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=> d his
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inventor search

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     (FILE 'STNGUIDE' ENTERED AT 09:56:52 ON 03 DEC 2001)
                DEL HIS Y

     FILE 'HCAPLUS, WPIDS, MEDLINE, BIOSIS' ENTERED AT 10:04:53 ON 03 DEC 2001
                E BAR OR D/AU
L1             93 S E3-4
                E LAU E/AU
L2            469 S E3-23
L3             42 S E40-45
L4            585 S L1 OR L2 OR L3
L5             12 S L4 AND RADICAL?
L6             39 S L4 AND ALBUMIN?
L7              7 S L5 AND L6
L8              3 DUP REM L7 (4 DUPLICATES REMOVED)
L9        1161485 S OXYGEN OR OXIDATIVE?
L10            16 S L4 AND L9
L11             6 S L10 AND L6
L12             3 DUP REM L11 (3 DUPLICATES REMOVED)
L13             4 S L12 OR L8

=> d all 1-13

L13  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2001 ACS
AN   2001:416050  HCAPLUS
DN   135:193981
TI   An Analog of the Human Albumin N-Terminus (Asp-Ala-His-Lys)
     Prevents Formation of Copper-Induced Reactive Oxygen Species
AU   Bar-Or, David; Rael, Leonard T.; Lau, Edward P.; Rao,
     Nagaraja K. R.; Thomas, Gregory W.; Winkler, James V.; Yukl, Richard L.;
     Kingston, Robert G.; Curtis, C. Gerald
CS   Department of Trauma Research, Swedish Medical Center, Englewood, CO,
     80110, USA
SO   Biochem. Biophys. Res. Commun. (2001), 284(3), 856-862
     CODEN: BBRCA9; ISSN: 0006-291X
PB   Academic Press
DT   Journal
LA   English
CC   14-15 (Mammalian Pathological Biochemistry)
AB   Copper mobilization and redox activity form damaging reactive oxygen
     species (ROS) and are implicated in the pathogenesis of ischemia
     -reperfusion injury, chronic inflammation, Alzheimer's disease, aging, and
     cancer. Protein sequestration of Cu(II) ions has been shown to prevent
     ROS-generating reactions. The first four amino acids of the N-terminus of
     human albumin, Asp-Ala-His-Lys (DAHK), form a tight binding site for
     Cu(II) ions. We synthesized several analogs, including the enantiomer
     d-DAHK, to study their effects on copper-induced hydroxyl radical and
     superoxide formation in the presence of ascorbate. D-DAHK prevented
     thiobarbituric acid-reactive species (TBARS) formation within physiol. and
     acidic pH ranges (7.5-6.5) and inhibited low-d. lipoprotein lipid
     peroxidn. A d-DAHK/Cu complex exhibited superoxide dismutase-like
     activity by significantly inhibiting superoxide formation. These in vitro
     results suggest that d-DAHK may shift the Cu(II)-binding equil. from the
     exchangeable Cu(II) pool to the tightly-bound, nonexchangeable pool,
     prevent ROS formation, and potentially provide therapeutic benefit for
     ROS-related diseases. (c) 2001 Academic Press.
ST   human albumin N terminus copper induced reactive oxygen
     species
IT   Albumins, biological studies
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RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(N-terminus Asp-Ala-His-Lys; analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT Protein motifs
(N-terminus of human **albumin**; analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT Ischemia
**Oxidative** stress, biological
(analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT Reactive **oxygen** species
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT Reperfusion
(injury; analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT Disease, animal
(reactive **oxygen** species-related; analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT 7440-50-8, Copper, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT 7782-44-7D, **Oxygen, radicals**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT 3352-57-6, Hydroxyl, biological studies 11062-77-4, Superoxide anion
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

IT 50-81-7, Ascorbic acid, biological studies 111543-77-2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(analog of human **albumin** N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive **oxygen** species)

RE.CNT 52
RE

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L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:241618 HCAPLUS
DN 132:276296
TI Tests and kits for the rapid evaluation of ischemic states by measuring altered serum **albumins**
IN **Bar-or, David**; **Lau, Edward**; Winkler, James V.
PA Ischemia Technologies, Inc., USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N021-00
ICS G01N021-29; G01N031-22; G01N033-543; G01N033-00; G01N033-53; C12Q001-00
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 14
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000020840 | A1 | 20000413 | WO 1999-US22905 | 19991001 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,

MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9964095 A1 20000426 AU 1999-64095 19991001
EP 1125107 A1 20010822 EP 1999-951710 19991001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1998-102738 P 19981002
US 1998-165581 A2 19981002
US 1998-165926 A2 19981002
US 1999-115392 P 19990111
WO 1999-US22905 W 19991001

AB The present invention relates to rapid methods for the detection of ischemic states and to kits for use in such methods. Provided for is a rapid method of testing for and quantifying ischemia based upon methods of detecting and quantifying the existence of an alteration of the serum protein albumin which occurs following an ischemic event; methods for detecting and quantifying this alteration include evaluating and quantifying the cobalt binding capacity of circulating albumin, anal. and measurement of the ability of serum albumin to bind exogenous cobalt, detection and measurement of the presence of endogenous copper in a purified albumin sample and use of an immunol. assay specific to the altered form of serum albumin which occurs following an ischemic event. Also taught by the present invention is the detection and measurement of an ischemic event by measuring albumin N-terminal derivs. that arise following an ischemic event, including truncated albumin species lacking one to four N-terminal amino acids or albumin with an acetylated N-terminal Asp residue. Patient sera was added to two tubes contg. CoCl2. After reaction, dithiothreitol was added to one of the tubes and NaCl was added to both. A470 spectroscopy measurements were taken of the two tubes.

ST serum **albumin** detn ischemia; cobalt serum **albumin** spectroscopy ischemia; copper serum **albumin** ischemia

IT Heart
(ECG; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Amniotic fluid
Biological materials
Body fluid
Cerebrospinal fluid
Lymph
Saliva
(anal. of; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Heart, disease
(angina pectoris; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Artery
(angioplasty, assessing efficacy of; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Heart, disease
(arrhythmia; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Calibration
(compn. for; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Ligands
RL: ARG (Analytical reagent use); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(immobilized, to **albumin**; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(immobilized; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Heart, disease
(infarction; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Salts, biological studies
RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(metal ion; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Antibodies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(monoclonal, to human serum **albumin** N-terminal derivs.; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT **Albumins**, analysis
RL: ANT (Analyte); BOC (Biological occurrence); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(serum; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Atomic absorption spectrometry
Atomic emission spectrometry
Blood analysis
Color formers
Diagnosis
Exercise
Filters
Immunoassay
Ischemia
Test kits
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT Antibodies
RL: ARG (Analytical reagent use); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 263740-32-5, 5-585-Serum **albumin** (human) 263740-33-6, 3-585-Serum **albumin** (human) 263740-34-7, 2-585-Serum **albumin** (human) 263740-35-8, Serum **albumin** (human) 263740-36-9, 4-585-Serum **albumin** (human)
RL: ANT (Analyte); BPR (Biological process); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(amino acid sequence, monoclonal antibody to N-terminus of; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 111543-77-2D, salts or complexes
RL: ARG (Analytical reagent use); BPR (Biological process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC

(Process); USES (Uses)
(antibody to or color-forming compds. contg.; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 7782-44-7, **Oxygen**, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(cobalt binding to octapeptide enhancement by; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 263562-84-1
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process)
(cobalt ion reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 263562-85-2P 263562-86-3P
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(cobalt ion reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 541-50-4D, derivs. 13598-36-2D, Phosphonic acid, derivs.
RL: DEV (Device component use); USES (Uses)
(matrix, as support; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 111543-77-2
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(nickel and copper ions reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 263562-87-4 263562-88-5 263562-89-6
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(nickel ion reactivity with; tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 7440-50-8D, Copper, salts or ions or complexes with human serum **albumin**
RL: ANT (Analyte); ARG (Analytical reagent use); BPR (Biological process); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 7646-79-9, Cobalt chloride, biological studies 7718-54-9, Nickel chloride, biological studies 7758-98-7, Sulfuric acid copper(2+) salt (1:1), biological studies
RL: ARG (Analytical reagent use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)

IT 7439-89-6D, Iron, salts 7439-92-1D, Lead, salts 7439-96-5D, Manganese, salts 7439-97-6D, Mercury, salts 7439-98-7D, Molybdenum, salts 7440-02-0D, Nickel, salts or support-immobilized 7440-22-4D, Silver, salts 7440-36-0D, Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4D, Cobalt, salts or support-immobilized 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts 7440-66-6D, Zinc, salts
RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
IT 134872-38-1
RL: PRP (Properties); RCT (Reactant)
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
IT 263562-90-9P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(tests and kits for rapid evaluation of ischemic states by measuring altered serum **albumins**)
RE.CNT 2
RE
(1) Bar-Or; US 5227307 A 1993
(2) Bar-Or; US 5290519 A 1994

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:241285 HCAPLUS
DN 132:276307
TI Methods and materials for detection and measurement of free **radical** damage
IN **Bar-Or, David; Lau, Edward**
PA Diagnostic Markers, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-47
ICS C07K016-06; G01N033-534
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 14

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000020454 | A1 | 20000413 | WO 1999-US22746 | 19991001 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9962793 | A1 | 20000426 | AU 1999-62793 | 19991001 |
| EP 1117686 | A1 | 20010725 | EP 1999-950055 | 19991001 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI US 1998-102962 | P | 19981002 | | |
| US 1998-165961 | A | 19981002 | | |
| WO | W | 19991001 | | |

AB The [illegible] a marker useful for detection and mea[illegible]ecifically, the invention takes adv[illegible] the N-terminus of the albumin mo[illegible]ood, in the presence of free ra[illegible] ability of the N-terminus of the al[illegible]or detecting and quantifying this al[illegible]tifying the cobalt binding capacity o[illegible] measurement of the ability of a[illegible]ction and measurement of the p[illegible]in sample and use of an immunol.

5,227,307

assay specific to the altered form of serum albumin which occurs following free radical damage. Also taught by the present invention is the use of the peptide Asp Ala His Lys and the compd. Asp-Ala-His-Lys-R, wherein R is any chem. group capable of producing a detectable signal when a metal ion capable of binding to the N-terminus of naturally-occurring albumin is bound to the compd., for detection and quantitation of the marker. Methods of the present invention also include use of the marker as a "biochem. tag", thereby allowing for sensitive detection and measurement of the efficacy of clin. drugs and therapeutics which result in the generation of free radicals or which act to limit free radical damage. The marker also acts as a "biol. tag" of a process implicated in a wide array of diseases and conditions and, accordingly, may be used to monitor and assess such diseases and conditions. Finally, the invention provides antibodies, immunoassays, and kits for use in detecting or quantitating the marker.

ST detection free **radical** damage

IT **Radicals**, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(damage; methods and materials for detection and measurement of free **radical** damage)

IT Transition metals, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ions; methods and materials for detection and measurement of free **radical** damage)

IT Atomic absorption spectrometry
Atomic emission spectrometry
Containers
Disease, animal
Drugs
Immunoassay
Test kits
Therapy
(methods and materials for detection and measurement of free **radical** damage)

IT Antibodies
RL: ANT (Analyte); ANST (Analytical study)
(methods and materials for detection and measurement of free **radical** damage)

IT **Albumins**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free **radical** damage)

IT Metals, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free **radical** damage)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free **radical** damage)

IT Periodic system
(salt of transition metal ions; methods and materials for detection and measurement of free **radical** damage)

IT **Albumins**, biological studies
**Albumins**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum; methods and materials for detection and measurement of free **radical** damage)

IT 7439-89-6D, Iron, salts 7439-92-1D, Lead, salts 7439-96-5D, Manganese, salts 7439-97-6D, Mercury, salts 7439-98-7D, Molybdenum, salts

7440-02-0D, Nickel, salts 7440-22-4D, Silver, salts 7440-36-0D, Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4, Cobalt, biological studies 7440-48-4D, Cobalt, salts 7440-50-8D, Copper, salts 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts 7440-66-6D, Zinc, salts 111543-77-2, Asp-Ala-His-Lys
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free **radical** damage)

IT 134872-38-1 263698-69-7
RL: PRP (Properties)
(unclaimed sequence; methods and materials for detection and measurement of free **radical** damage)

RE.CNT 3

RE

(1) Cotelle, N; Journal of Inorganic Biochemistry 1992, V46, P7 HCAPLUS
(2) Keller, R; Chem Res Toxicol 1993, V6(4), P430 HCAPLUS
(3) Laussac, J; Biochemistry 1984, V23(12), P2832 HCAPLUS

L13 ANSWER 4 OF 4 MEDLINE

AN 2001166045 MEDLINE
DN 21164743 PubMed ID: 11264015

TI Asp-Ala-His-Lys (DAHK) inhibits copper-induced **oxidative** DNA double strand breaks and telomere shortening.

AU **Bar-Or D**; Thomas G W; Rael L T; **Lau E P**; Winkler J V
CS Trauma Research, Swedish Medical Center, Englewood, Colorado, 80110, USA.. dbaror@dmibio.com

SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Mar 23) 282 (1) 356-60.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010417
Last Updated on STN: 20010417
Entered Medline: 20010412

AB Both DNA and the telomeric sequence are susceptible to copper-mediated reactive **oxygen** species (ROS) damage, particularly damage attributed to hydroxyl **radicals**. In this study, ROS-induced DNA double strand breaks and telomere shortening were produced by exposure to copper and ascorbic acid. Asp-Ala-His-Lys (DAHK), a specific copper chelating tetrapeptide d-analog of the N-terminus of human **albumin** , attenuated DNA strand breaks in a dose dependent manner. d-DAHK, at a ratio of 4:1 (d-DAHKCu), provided complete protection of isolated DNA from double strand breaks and, at a ratio of 2:1 (d-DAHKCu), completely protected DNA in Raji cells exposed to copper/ascorbate. Southern blots of DNA treated with copper/ascorbate showed severe depletion and shortening of telomeres and Raji cell treated samples showed some conservation of telomere sequences. d-DAHK provided complete telomere length protection at a ratio of 2:1 (d-DAHKCu). The human **albumin** N-terminus analog, d-DAHK, protects DNA and telomeres against copper-mediated ROS damage and may be a useful therapeutic adjunct in ROS disease processes. Copyright 2001 Academic Press.

CT Check Tags: Human; Support, Non-U.S. Gov't
Cell Line
*Copper: AI, antagonists & inhibitors
Copper: PD, pharmacology
DNA: DE, drug effects

*DNA Damage
*Oligopeptides: PD, pharmacology
***Oxidative Stress**
*Telomere: DE, drug effects
RN 7440-50-8 (Copper); 9007-49-2 (DNA)
CN 0 (Oligopeptides)

sequence search on STN

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=> d his

     (FILE 'WPIDS' ENTERED AT 09:31:09 ON 03 DEC 2001)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 09:33:11 ON 03 DEC 2001
L1            88 S ^DAHK/SQSP
L2            19 S L1 AND SQL=4

     FILE 'HCAPLUS' ENTERED AT 09:34:32 ON 03 DEC 2001
L3            13 S L2
L4             4 S L3 AND RADICAL?
L5             4 S L1 AND RADICAL?
L6             4 S L4 OR L5

=> d .ca l6 1-4

L6   ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:416050  HCAPLUS
DOCUMENT NUMBER:          135:193981
TITLE:                    An Analog of the Human Albumin N-Terminus
                          (Asp-Ala-His-Lys) Prevents Formation of Copper-Induced
                          Reactive Oxygen Species
AUTHOR(S):                Bar-Or, David; Rael, Leonard T.; Lau, Edward P.; Rao,
                          Nagaraja K. R.; Thomas, Gregory W.; Winkler, James V.;
                          Yukl, Richard L.; Kingston, Robert G.; Curtis, C.
                          Gerald
CORPORATE SOURCE:         Department of Trauma Research, Swedish Medical Center,
                          Englewood, CO, 80110, USA
SOURCE:                   Biochem. Biophys. Res. Commun. (2001), 284(3), 856-862
                          CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER:                Academic Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Copper mobilization and redox activity form damaging reactive oxygen
     species (ROS) and are implicated in the pathogenesis of ischemia
     -reperfusion injury, chronic inflammation, Alzheimer's disease, aging, and
     cancer.  Protein sequestration of Cu(II) ions has been shown to prevent
     ROS-generating reactions.  The first four amino acids of the N-terminus of
     human albumin, Asp-Ala-His-Lys (DAHK), form a tight binding site for
     Cu(II) ions.  We synthesized several analogs, including the enantiomer
     d-DAHK, to study their effects on copper-induced hydroxyl radical and
     superoxide formation in the presence of ascorbate.  D-DAHK prevented
     thiobarbituric acid-reactive species (TBARS) formation within physiol. and
     acidic pH ranges (7.5-6.5) and inhibited low-d. lipoprotein lipid
     peroxidn.  A d-DAHK/Cu complex exhibited superoxide dismutase-like
     activity by significantly inhibiting superoxide formation.  These in vitro
     results suggest that d-DAHK may shift the Cu(II)-binding equil. from the
     exchangeable Cu(II) pool to the tightly-bound, nonexchangeable pool,
     prevent ROS formation, and potentially provide therapeutic benefit for
     ROS-related diseases.  (c) 2001 Academic Press.
CC   14-15 (Mammalian Pathological Biochemistry)
IT   7782-44-7D, Oxygen, radicals
     RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
     BIOL (Biological study); OCCU (Occurrence)
        (analog of human albumin N-terminus (Asp-Ala-His-Lys) prevents
        formation of copper-induced reactive oxygen species)
IT   50-81-7, Ascorbic acid, biological studies 111543-77-2
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
```

(analog of human albumin N-terminus (Asp-Ala-His-Lys) prevents formation of copper-induced reactive oxygen species)

REFERENCE COUNT: 52

REFERENCE(S):
(1) Athar, M; Biochem Mol Biol Int 1996, V39, P813 HCAPLUS
(2) Bar-Or, D; Am Heart J 2001, V141, P985 HCAPLUS
(3) Bar-Or, D; Eur J Biochem 2001, V268, P42 HCAPLUS
(5) Beauchamp, C; Anal Biochem 1971, V44, P276 HCAPLUS
(6) Belayev, L; Stroke 2001, V32, P553 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:265447 HCAPLUS

DOCUMENT NUMBER: 134:290423

TITLE: Metal-binding peptide compounds for reducing the damage done by reactive oxygen species and reducing the concn. of a metal in an animal

INVENTOR(S): Bar-Or, David; Curtis, C. Gerald; Lau, Edward; Rao, Nagaraja K. R.; Winkler, James V.; Crook, Wannell M.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001025265 | A1 | 20010412 | WO 2000-US26952 | 20000929 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-157404 P 19991001
US 2000-211078 P 20000613

AB A method is provided for reducing the damage done by reactive oxygen species (ROS) in an animal. The invention also provides a method of reducing the concn. of a metal in an animal. These methods comprise administering to the animal an effective amt. of a metal-binding peptide compd. The invention further provides a method of reducing the damage done by ROS in a tissue or an organ that has been removed from an animal. The method comprises contacting the tissue or organ with a soln. contg. an effective amt. of a metal-binding peptide compd. of the invention. The invention further provides metal-binding peptide compds., pharmaceutical compns., and kits.

IC ICM C07K007-00

CC 1-12 (Pharmacology)
Section cross-reference(s): 34, 63

IT 3352-57-6, Hydroxyl **radical**, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT 71-00-1, Histidine, biological studies **111543-77-2D**, copper complexes
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT **111543-77-2P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT **263562-85-2 263562-86-3** 263562-87-4 263562-88-5
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT **333952-24-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

IT 81748-02-9P **333952-21-9P 333952-22-0P**
**333952-23-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(metal-binding peptide compds. for redn. of damage done by reactive oxygen species and redn. of concn. of metal in animal)

REFERENCE COUNT: 1
REFERENCE(S): (1) Pallenberg; US 5538945 A 1996 HCAPLUS

L6 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:241285 HCAPLUS
DOCUMENT NUMBER: 132:276307
TITLE: Methods and materials for detection and measurement of free **radical** damage
INVENTOR(S): Bar-Or, David; Lau, Edward
PATENT ASSIGNEE(S): Diagnostic Markers, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000020454 | A1 | 20000413 | WO 1999-US22746 | 19991001 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
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| AU 9962793 | A1 | 20000426 | AU 1999-62793 | 19991001 |
| EP 1117686 | A1 | 20010725 | EP 1999-950055 | 19991001 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1998-102962 P 19981002
US 1998-165961 A 19981002
WO 1999-US22746 W 19991001

AB The present invention teaches a marker useful for detection and measurement of free radical damage. Specifically, the invention takes advantage of alterations which occur to the N-terminus of the albumin mol., a circulating protein in human blood, in the presence of free radicals. These alterations effect the ability of the N-terminus of the albumin mol. to bind metals. Methods for detecting and quantifying this alteration include evaluating and quantifying the cobalt binding capacity of an albumin-contg. sample, anal. and measurement of the ability of albumin to bind exogenous cobalt, detection and measurement of the presence of copper in a purified albumin sample and use of an immunol. assay specific to the altered form of serum albumin which occurs following free radical damage. Also taught by the present invention is the use of the peptide Asp Ala His Lys and the compd. Asp-Ala-His-Lys-R, wherein R is any chem. group capable of producing a detectable signal when a metal ion capable of binding to the N-terminus of naturally-occurring albumin is bound to the compd., for detection and quantitation of the marker. Methods of the present invention also include use of the marker as a "biochem. tag", thereby allowing for sensitive detection and measurement of the efficacy of clin. drugs and therapeutics which result in the generation of free radicals or which act to limit free radical damage. The marker also acts as a "biol. tag" of a process implicated in a wide array of diseases and conditions and, accordingly, may be used to monitor and assess such diseases and conditions. Finally, the invention provides antibodies, immunoassays, and kits for use in detecting or quantitating the marker.

IC ICM C07K014-47
ICS C07K016-06; G01N033-534
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 14
ST detection free **radical** damage

IT **Radicals**, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(damage; methods and materials for detection and measurement of free **radical** damage)

IT Transition metals, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ions; methods and materials for detection and measurement of free **radical** damage)

IT Atomic absorption spectrometry
Atomic emission spectrometry
Containers
Disease, animal
Drugs
Immunoassay
Test kits
Therapy
(methods and materials for detection and measurement of free **radical** damage)

IT Antibodies
RL: ANT (Analyte); ANST (Analytical study)
(methods and materials for detection and measurement of free **radical** damage)

IT Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free

**radical** damage)

IT Metals, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free **radical** damage)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free **radical** damage)

IT Periodic system
(salt of transition metal ions; methods and materials for detection and measurement of free **radical** damage)

IT Albumins, biological studies
Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum; methods and materials for detection and measurement of free **radical** damage)

IT 7439-89-6D, Iron, salts 7439-92-1D, Lead, salts 7439-96-5D, Manganese, salts 7439-97-6D, Mercury, salts 7439-98-7D, Molybdenum, salts 7440-02-0D, Nickel, salts 7440-22-4D, Silver, salts 7440-36-0D, Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4, Cobalt, biological studies 7440-48-4D, Cobalt, salts 7440-50-8D, Copper, salts 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts 7440-66-6D, Zinc, salts **111543-77-2**, Asp-Ala-His-Lys
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of free **radical** damage)

IT **134872-38-1** 263698-69-7
RL: PRP (Properties)
(unclaimed sequence; methods and materials for detection and measurement of free **radical** damage)

REFERENCE COUNT: 3
REFERENCE(S):
(1) Cotelle, N; Journal of Inorganic Biochemistry 1992, V46, P7 HCAPLUS
(2) Keller, R; Chem Res Toxicol 1993, V6(4), P430 HCAPLUS
(3) Laussac, J; Biochemistry 1984, V23(12), P2832 HCAPLUS

L6 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:402510 HCAPLUS
DOCUMENT NUMBER: 117:2510
TITLE: Redox chemistry of complexes of nickel(II) with some biologically important peptides in the presence of reduced oxygen species: an ESR study
AUTHOR(S): Cotelle, N.; Tremolieres, E.; Bernier, J. L.; Catteau, J. P.; Henichart, J. P.
CORPORATE SOURCE: INSERM, Lille, 59045, Fr.
SOURCE: J. Inorg. Biochem. (1992), 46(1), 7-15
CODEN: JIBIDJ; ISSN: 0162-0134
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The reactions between some Ni(II) oligopeptides (Gly-His-Lys, (Gly)4, Asp-Ala-His-Lys, Gly-Gly-His, .beta.Ala-His, and serum albumin) and reduced oxygen species were characterized by spin-trapping expts. using DMPO and Me2SO. Most of the peptides possessed superoxide dismutase- and catalase-like activities leading to the formation of either oxene [NiO]2+ or, in the case of .beta.Ala-His, hydroxyl radicals. Both these species may affect DNA integrity through distinct mechanisms.

CC 4-6 (Toxicology)
IT 3352-57-6, Hydroxylradical, reactions 7722-84-1, Hydrogen peroxide, biological studies 7782-44-7D, Oxygen, **radicals** 11062-77-4, Superoxide anion
RL: RCT (Reactant)
(reaction of, with nickel-oligopeptide complexes)
IT 305-84-0D, nickel complexes 7440-02-0D, Nickel, oligopeptide complexes 7451-76-5D, nickel complexes 39016-92-7 49557-75-7D, nickel complexes **111543-77-2D**, nickel complexes
RL: RCT (Reactant)
(reaction of, with reactive oxygen species)

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E1 THROUGH E48 ASSIGNED

=> select rn l6 1-4 hit
E49 THROUGH E56 ASSIGNED

=> fil reg
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


STRUCTURE FILE UPDATES: 30 NOV 2001 HIGHEST RN 372937-30-9
DICTIONARY FILE UPDATES: 30 NOV 2001 HIGHEST RN 372937-30-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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(111543-77-2/RN)
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L8             8 L7 AND L1

=> d sqide3 1-8

L8   ANSWER 1 OF 8  REGISTRY  COPYRIGHT 2001 ACS
RN   333952-24-2  REGISTRY
CN   D-Lysine, D-.alpha.-aspartyl-D-alanyl-D-histidyl- (9CI)  (CA INDEX NAME)
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  4

SEQ3      1 Asp-Ala-His-Lys
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Absolute stereochemistry.
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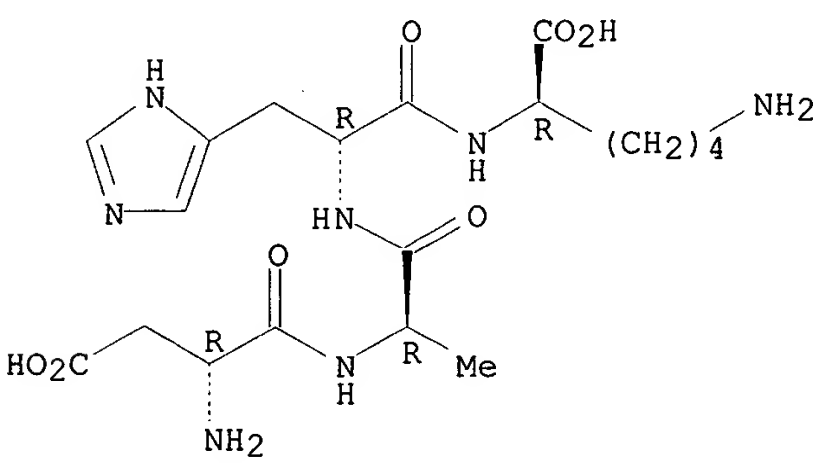


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             2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8   ANSWER 2 OF 8  REGISTRY  COPYRIGHT 2001 ACS
RN   333952-23-1  REGISTRY
CN   L-Lysine, N,N-bis[2-(2-pyridinyl)ethyl]-L-.alpha.-aspartyl-L-alanyl-L-
     histidyl-N6,N6-bis[2-(2-pyridinyl)ethyl]- (9CI)  (CA INDEX NAME)
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  4
NTE  modified
-------------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------------
modification     Asp-1              -          undetermined modification
modification     Lys-4              -          undetermined modification
-------------------------------------------------------------------------

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Absolute stereochemistry.

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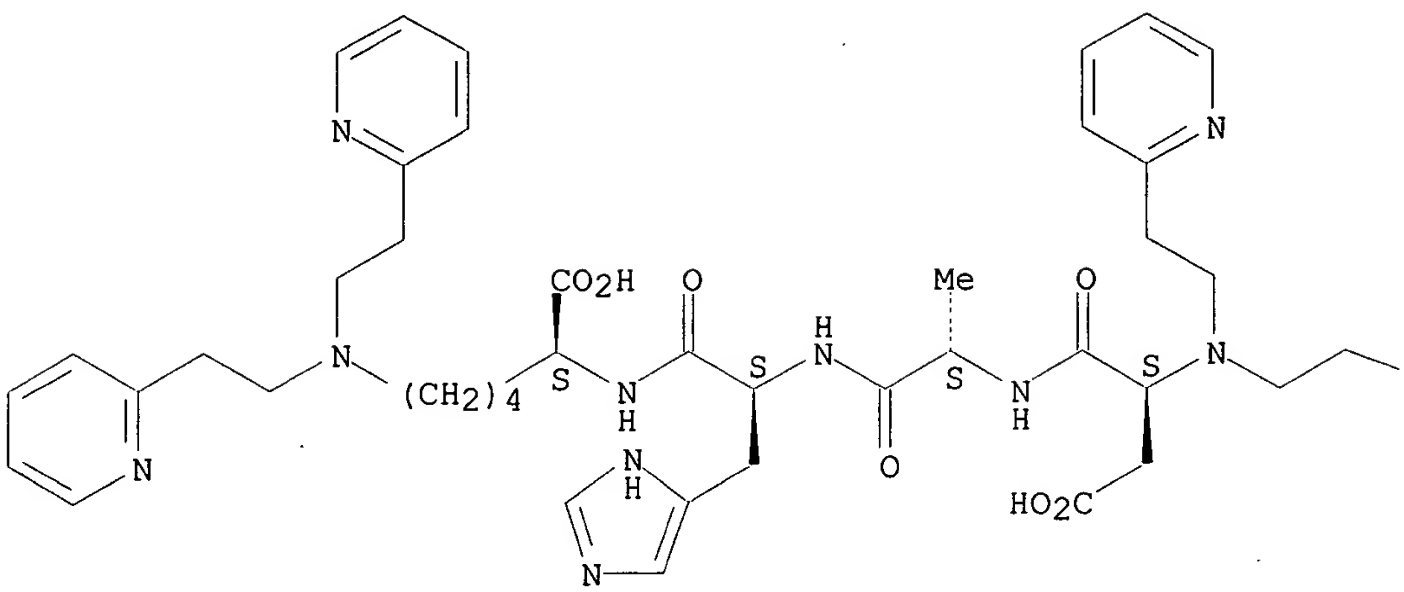

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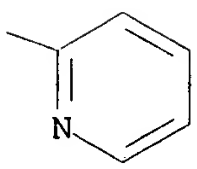

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN **333952-22-0** REGISTRY
CN L-Lysine, 4,4'-[(7,12-diethyl-3,8,13,17-tetramethyl-21H,23H-porphine-2,18-diyl)bis(1-oxo-3,1-propanediyl)]bis[L-.alpha.-aspartyl-L-alanyl-L-histidyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8,4,4
NTE multichain
modified (modifications unspecified)

| type | ------ location ------ | description |
|---|---|---|
| bridge | Lys-4 - Lys-4' | covalent bridge, dimer |

SEQ3 1 Asp-Ala-His-Lys
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HITS AT: 1-4

SEQ3 1 Asp-Ala-His-Lys
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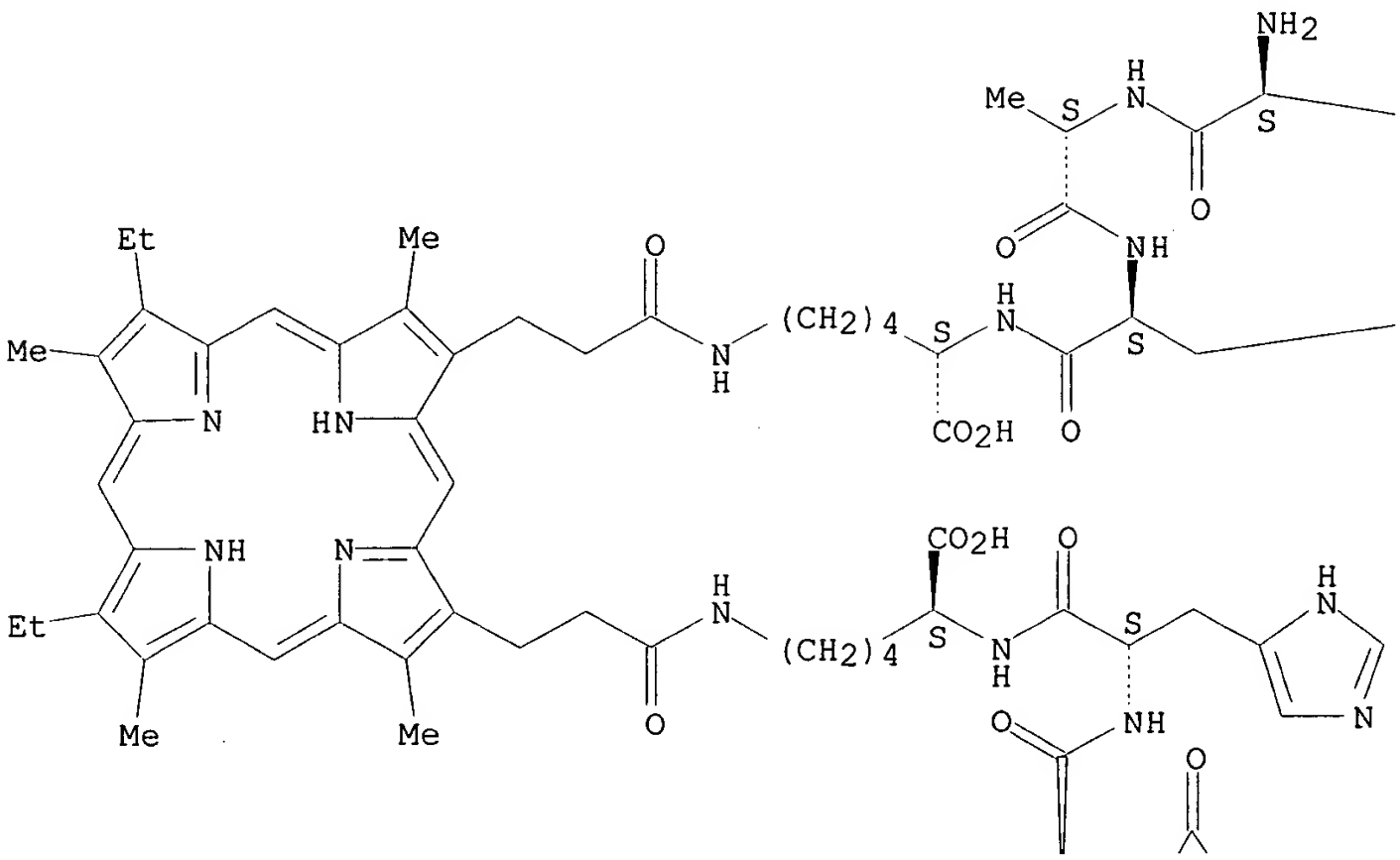
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.

PAGE 1-A



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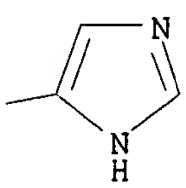

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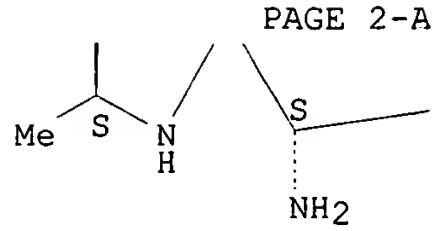


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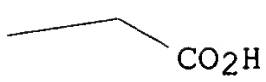


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN **333952-21-9** REGISTRY
CN L-Lysine, N,N-bis(carboxymethyl)-L-.alpha.-aspartyl-L-alanyl-L-histidyl-N6,N6-bis(carboxymethyl)- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 4
NTE modified (modifications unspecified)

SEQ3 1 Asp-Ala-His-Lys
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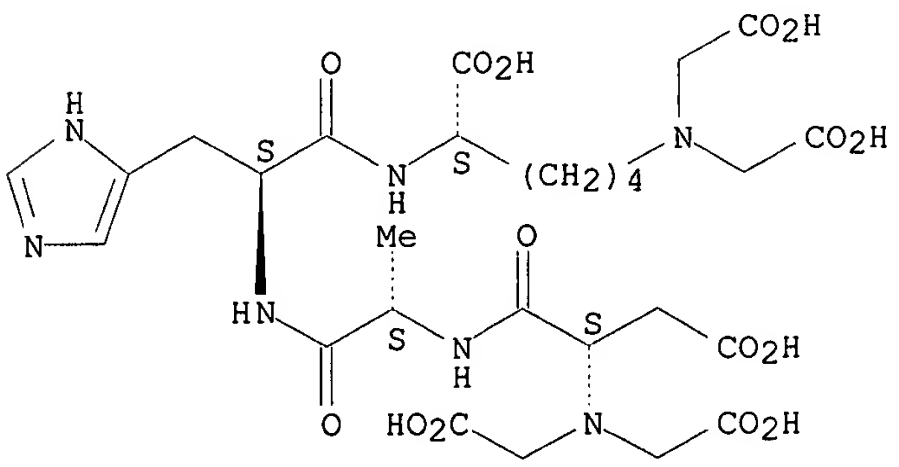
HITS AT: 1-4

MF C27 H39 N7 O15
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.




1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN **263562-86-3** REGISTRY
CN L-Lysine, N-acetyl-L-.alpha.-aspartyl-L-alanyl-L-histidyl-L-lysyl-L-seryl-L-.alpha.-glutamyl-L-valyl-L-alanyl-L-histidyl-L-arginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 12
NTE modified

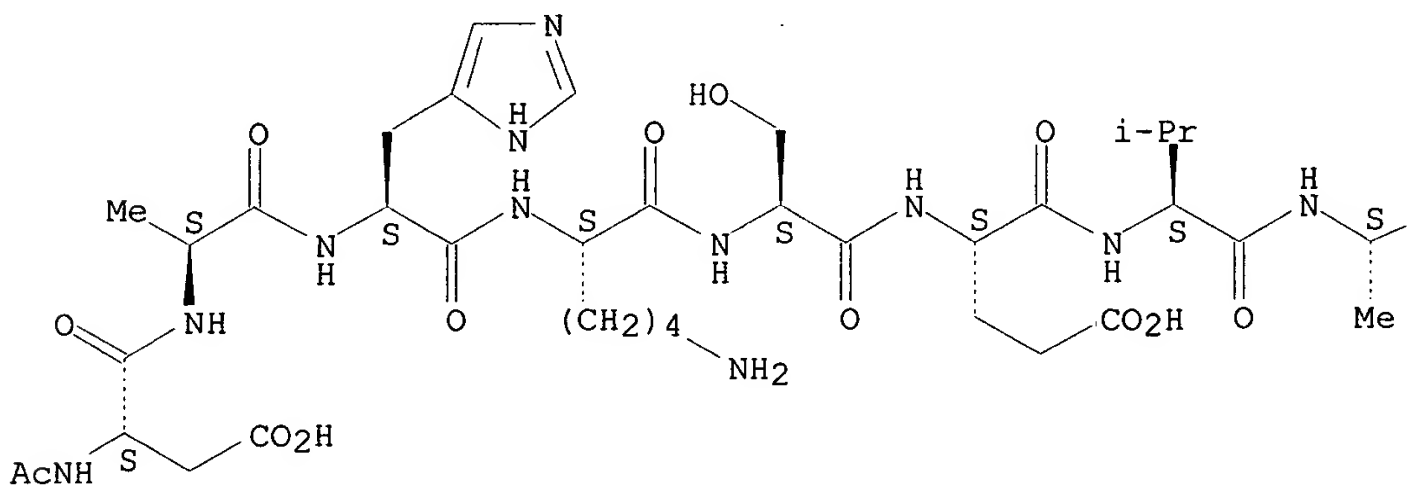
| type | location | description |
|---|---|---|
| terminal mod. | Asp-1 - | N-acetyl |

SEQ3 1 Asp-Ala-His-Lys-Ser-Glu-Val-Ala-His-Arg-
=== === === ===
11 Phe-Lys
HITS AT: 1-4

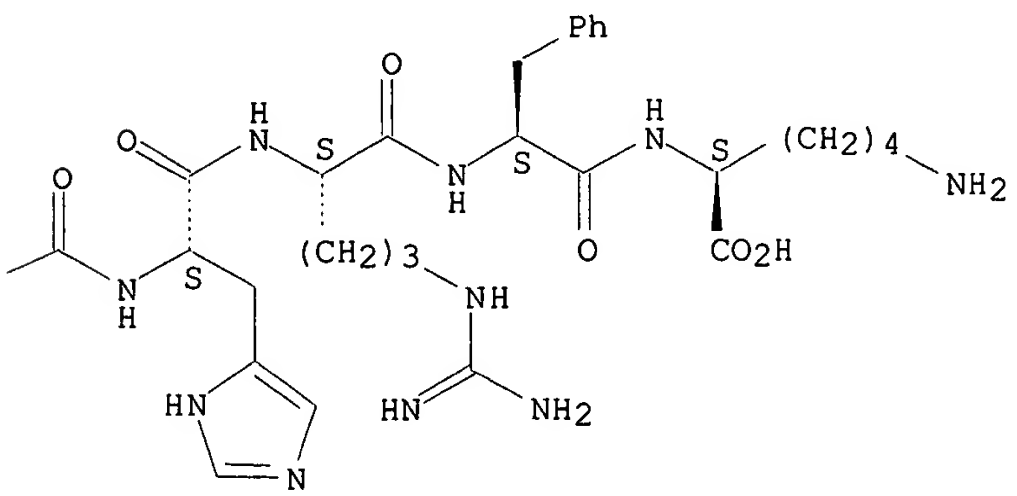
MF C64 H99 N21 O19
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

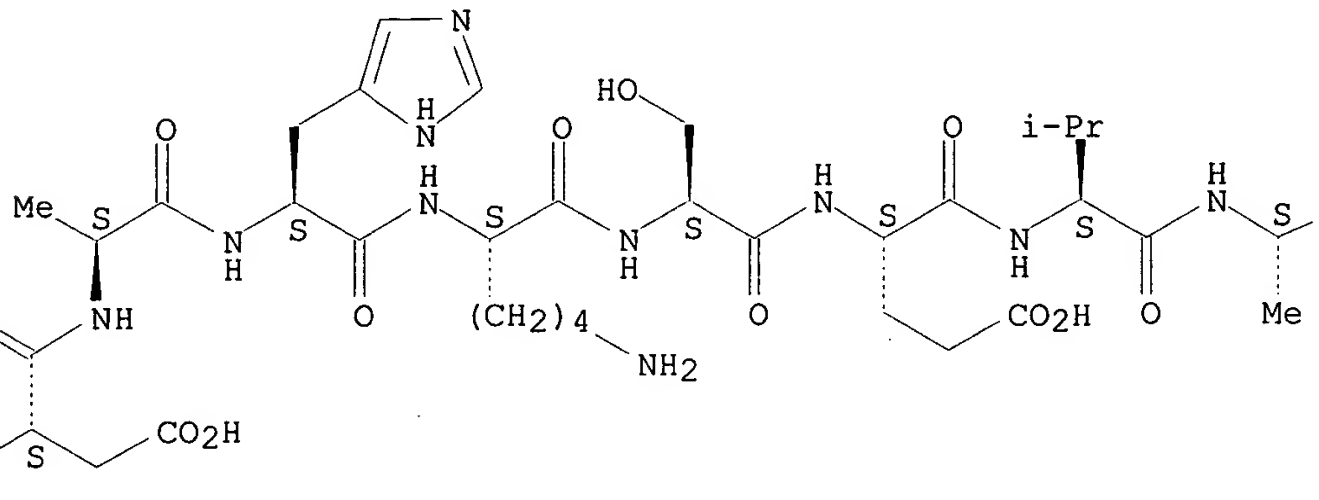
L8 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN **263562-85-2** REGISTRY
CN L-Lysine, L-.alpha.-aspartyl-L-alanyl-L-histidyl-L-lysyl-L-seryl-L-.alpha.-glutamyl-L-valyl-L-alanyl-L-histidyl-L-arginyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 12

SEQ3 1 Asp-Ala-His-Lys-Ser-Glu-Val-Ala-His-Arg-
=== === === ===
11 Phe-Lys
HITS AT: 1-4

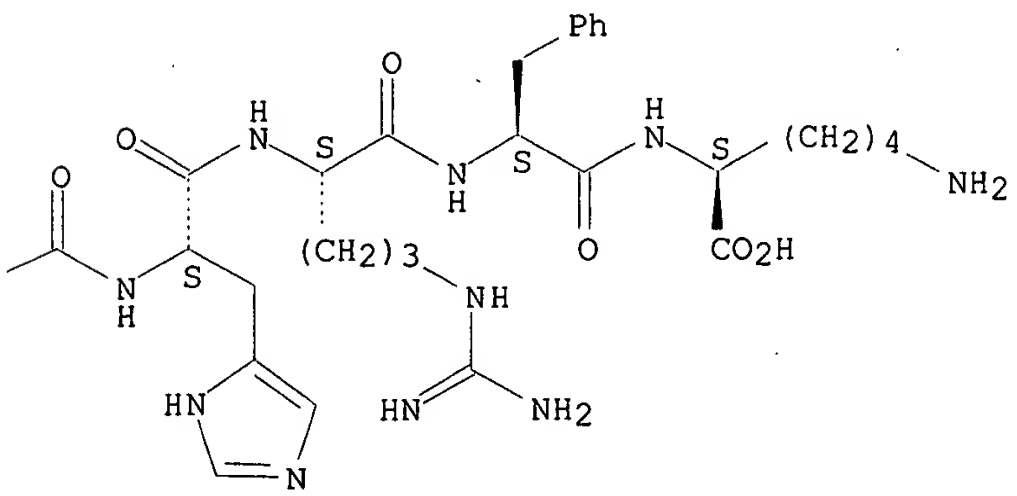
MF C62 H97 N21 O18
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



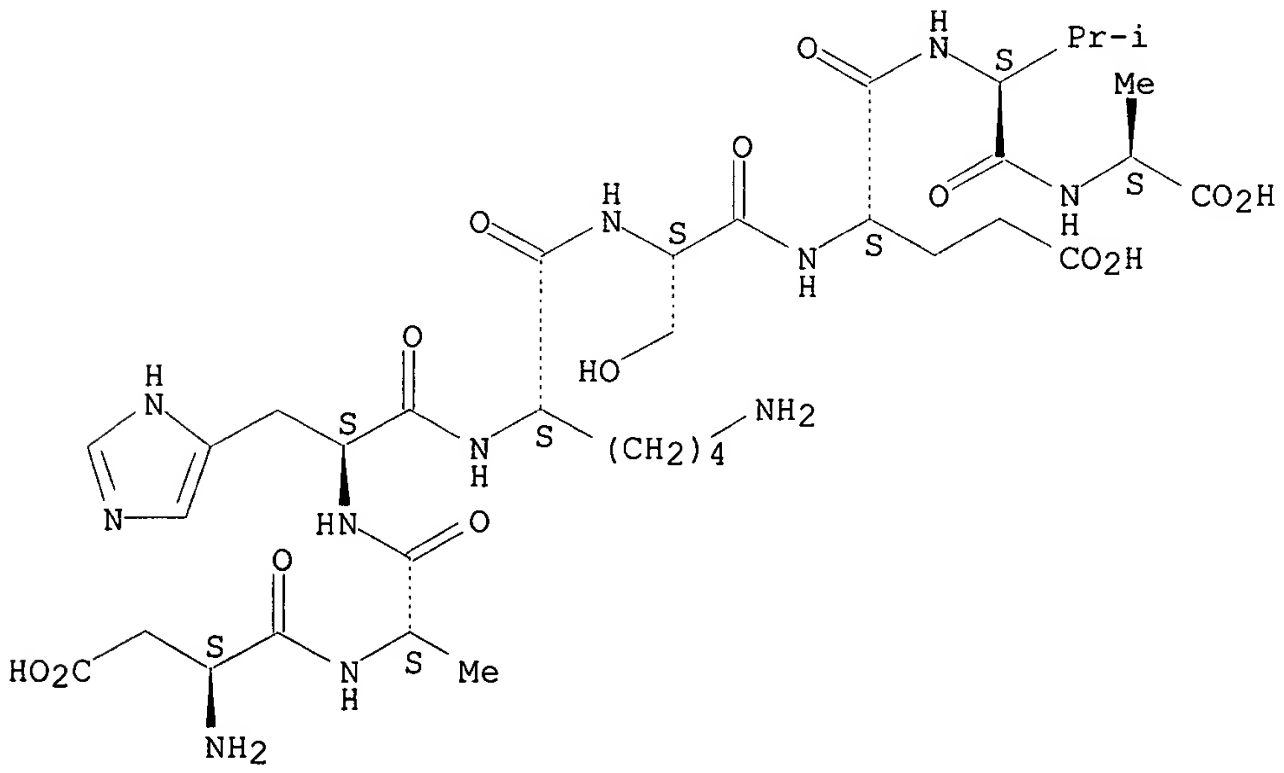
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L8 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN **134872-38-1** REGISTRY
CN L-Alanine, L-.alpha.-aspartyl-L-alanyl-L-histidyl-L-lysyl-L-seryl-L-.alpha.-glutamyl-L-valyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Alanine, N-[N-[N-[N-[N2-[N-(N-L-.alpha.-aspartyl-L-alanyl)-L-histidyl]-L-lysyl]-L-seryl]-L-.alpha.-glutamyl]-L-valyl]-
OTHER NAMES:
CN 1: PN: WO0020454 SEQID: 2 unclaimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ3 1 Asp-Ala-His-Lys-Ser-Glu-Val-Ala
=== === === ===
HITS AT: 1-4

MF C35 H57 N11 O14
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

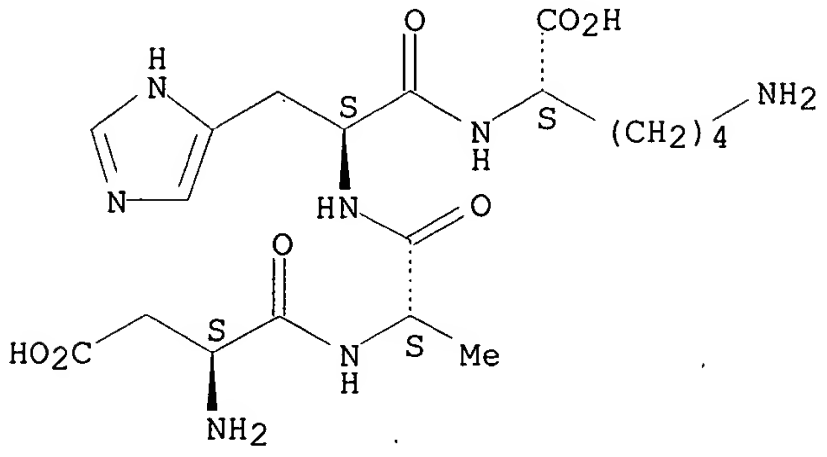
L8 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2001 ACS
RN **111543-77-2** REGISTRY
CN L-Lysine, L-.alpha.-aspartyl-L-alanyl-L-histidyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Lysine, N2-[N-(N-L-.alpha.-aspartyl-L-alanyl)-L-histidyl]-
OTHER NAMES:
CN 1: PN: WO0020454 SEQID: 1 claimed protein
CN Asp-Ala-His-Lys
FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 4

SEQ3 1 Asp-Ala-His-Lys
=== === === ===
HITS AT: 1-4

MF C19 H31 N7 O7
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, TOXCENTER, TOXLIT

Absolute stereochemistry.




9 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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L3          2911 S L1 (L) DAMAG?
L4         59348 S ALBUMIN?
L5           124 S L2  AND L4
L6            58 S L3 AND L4
L7           124 S L5 OR L5
L8           162 S L5 OR L6
L9       1090728 S METAL?
L10           11 S L9 AND L8

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                E PORFIMER SODIUM/CN
L12             1 S E3

     FILE 'HCAPLUS' ENTERED AT 09:21:14 ON 03 DEC 2001
L13           475 S L12 OR PORFIRMER?
L14             0 S L13 AND L8
L15        156256 S ANTIBOD?
L16         49177 S ATOMIC (L) SPECT?
L17             1 S L16 AND L8
L18             7 S L15 AND L8
L19         12045 S KIT#
L20        111553 S IMMUNOASSAY? OR ASSAY?
L21             5 S L8 AND (L19 OR L20)
L22            19 S L10 OR L17 OR L18 OR L21
L23            68 S L4 (L) L2
L24             7 S L23 (L) DAMAG?
L25            25 S L24 OR L22
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1947 - 3 Dec 2001  VOL 135 ISS 24
FILE LAST UPDATED: 2 Dec 2001  (20011202/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

 This file supports REGistRY for direct browsing and searching of
 all substance data from the REGISTRY file.  Enter HELP FIRST for
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HCAplus now provides online access to patents and literature covered
in CA from 1947 to the present.  On April 22, 2001, bibliographic
information and abstracts were added for over 2.2 million references
published in CA from 1947 to 1966.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE
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L3          2911 S L1 (L) DAMAG?
L4         59348 S ALBUMIN?
L5           124 S L2  AND L4
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L13           475 S L12 OR PORFIRMER?
L14             0 S L13 AND L8
L15        156256 S ANTIBOD?
L16         49177 S ATOMIC (L) SPECT?
L17             1 S L16 AND L8
L18             7 S L15 AND L8
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L19        12045 S KIT#
L20       111553 S IMMUNOASSAY? OR ASSAY?
L21            5 S L8 AND (L19 OR L20)
L22           19 S L10 OR L17 OR L18 OR L21
L23           68 S L4 (L) L2
L24            7 S L23 (L) DAMAG?
L25           25 S L24 OR L22

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=> d .ca 1-25

L25  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:293373  HCAPLUS
DOCUMENT NUMBER:          134:362454
TITLE:                    Structural damage to proteins caused by free radicals:
                          assessment, protection by antioxidants, and influence
                          of protein binding
AUTHOR(S):                Salvi, A.; Carrupt, P.-A.; Tillement, J.-P.; Testa, B.
CORPORATE SOURCE:         Section de Pharmacie, Institut de Chimie
                          Therapeutique, Universite de Lausanne, Lausanne,
                          CH-1015, Switz.
SOURCE:                   Biochem. Pharmacol. (2001), 61(10), 1237-1242
                          CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER:                Elsevier Science Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Oxidative damage to proteins results in biol. dysfunctions such as
     perturbed activity in enzymes, transport proteins, and receptors.  Here,
     the authors investigated structural damage to proteins induced by free
     radicals.  Structural alterations to lysozyme, human serum albumin (HSA)
     and .beta.-lactoglobulin A were monitored by capillary zone
     electrophoresis.  Four well-known antioxidants (quercetin, melatonin,
     Trolox, and chlorogenic acid) were examd. for their ability to inhibit
     protein damage and to bind to these proteins.  Melatonin and chlorogenic
     acid, which did not bind to any of the three proteins under study, showed
     scavenging and protective activities well correlated with the amt. of free
     radicals generated.  Trolox, which bound only to HSA, was a better
     protector of HSA than of the two other proteins, indicating that its
     antioxidant capacity is increased by a shielding effect.  Finally,
     quercetin was a good antioxidant in protecting lysozyme and
     .beta.-lactoglobulin A, but its binding to HSA resulted in a pro-oxidant
     effect that accelerated HSA fragmentation.  These results demonstrate that
     binding of an antioxidant to a protein may potentiate protection or damage
     depending on the properties of the antioxidant.
CC   4-3 (Toxicology)
IT   Albumins, biological studies
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (serum; structural damage to proteins caused by free
        radicals: assessment, protection by antioxidants, and influence
        of protein binding)
REFERENCE COUNT:          18
REFERENCE(S):             (1) Ahmed, M; Carcinogenesis 1994, V15, P1627 HCAPLUS
                          (2) Born, M; Helv Chim Acta 1996, V79, P1147 HCAPLUS
                          (3) Cao, G; Free Radic Biol Med 1997, V22, P749
                              HCAPLUS
                          (4) Davies, K; J Biol Chem 1987, V262, P8227 HCAPLUS
                          (5) Dean, R; Free Radic Res Commun 1989, V7, P97
                              HCAPLUS
                          ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

L25 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:241285 HCAPLUS
DOCUMENT NUMBER: 132:276307
TITLE: Methods and materials for detection and measurement of **free radical damage**
INVENTOR(S): Bar-Or, David; Lau, Edward
PATENT ASSIGNEE(S): Diagnostic Markers, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000020454 | A1 | 20000413 | WO 1999-US22746 | 19991001 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9962793 | A1 | 20000426 | AU 1999-62793 | 19991001 |
| EP 1117686 | A1 | 20010725 | EP 1999-950055 | 19991001 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.:
US 1998-102962 P 19981002
US 1998-165961 A 19981002
WO 1999-US22746 W 19991001

AB The present invention teaches a marker useful for detection and measurement of free radical damage. Specifically, the invention takes advantage of alterations which occur to the N-terminus of the albumin mol., a circulating protein in human blood, in the presence of free radicals. These alterations effect the ability of the N-terminus of the albumin mol. to bind metals. Methods for detecting and quantifying this alteration include evaluating and quantifying the cobalt binding capacity of an albumin-contg. sample, anal. and measurement of the ability of albumin to bind exogenous cobalt, detection and measurement of the presence of copper in a purified albumin sample and use of an immunol. assay specific to the altered form of serum albumin which occurs following free radical damage. Also taught by the present invention is the use of the peptide Asp Ala His Lys and the compd. Asp-Ala-His-Lys-R, wherein R is any chem. group capable of producing a detectable signal when a metal ion capable of binding to the N-terminus of naturally-occurring albumin is bound to the compd., for detection and quantitation of the marker. Methods of the present invention also include use of the marker as a "biochem. tag", thereby allowing for sensitive detection and measurement of the efficacy of clin. drugs and therapeutics which result in the generation of free radicals or which act to limit free radical damage. The marker also acts as a "biol. tag" of a process implicated in a wide array of diseases and conditions and, accordingly, may be used to monitor and assess such diseases and conditions. Finally, the invention provides antibodies, immunoassays, and kits for use in detecting or quantitating the marker.

IC ICM C07K014-47

ICS C07K016-06; G01N033-534
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 14
ST detection **free radical damage**
IT **Radicals**, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**damage**; methods and materials for detection and measurement of **free radical damage**)
IT Transition **metals**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ions; methods and materials for detection and measurement of **free radical damage**)
IT **Atomic** absorption **spectrometry**
**Atomic** emission **spectrometry**
Containers
Disease, animal
Drugs
**Immunoassay**
Test **kits**
Therapy
(methods and materials for detection and measurement of **free radical damage**)
IT **Antibodies**
RL: ANT (Analyte); ANST (Analytical study)
(methods and materials for detection and measurement of **free radical damage**)
IT **Albumins**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of **free radical damage**)
IT **Metals**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of **free radical damage**)
IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of **free radical damage**)
IT Periodic system
(salt of transition **metal** ions; methods and materials for detection and measurement of **free radical damage**)
IT **Albumins**, biological studies
**Albumins**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum; methods and materials for detection and measurement of **free radical damage**)
IT 7439-89-6D, Iron, salts 7439-92-1D, Lead, salts 7439-96-5D, Manganese, salts 7439-97-6D, Mercury, salts 7439-98-7D, Molybdenum, salts 7440-02-0D, Nickel, salts 7440-22-4D, Silver, salts 7440-36-0D, Antimony, salts 7440-38-2D, Arsenic, salts 7440-39-3D, Barium, salts 7440-43-9D, Cadmium, salts 7440-47-3D, Chromium, salts 7440-48-4, Cobalt, biological studies 7440-48-4D, Cobalt, salts 7440-50-8D, Copper, salts 7440-57-5D, Gold, salts 7440-62-2D, Vanadium, salts 7440-66-6D, Zinc, salts 111543-77-2, Asp-Ala-His-Lys
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and materials for detection and measurement of **free radical damage**)
IT 134872-38-1 263698-69-7
RL: PRP (Properties)

(unclaimed sequence; methods and materials for detection and measurement of **free radical damage**)

REFERENCE COUNT: 3
REFERENCE(S):
(1) Cotelle, N; Journal of Inorganic Biochemistry 1992, V46, P7 HCAPLUS
(2) Keller, R; Chem Res Toxicol 1993, V6(4), P430 HCAPLUS
(3) Laussac, J; Biochemistry 1984, V23(12), P2832 HCAPLUS

L25 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:94175 HCAPLUS
DOCUMENT NUMBER: 132:276022
TITLE: Increased oxidative modification of albumin when illuminated in vitro in the presence of a common sunscreen ingredient: protection by nitroxide radicals
AUTHOR(S): Damiani, E.; Carloni, P.; Biondi, C.; Greci, L.
CORPORATE SOURCE: Dipartimento di Scienze dei Materiali e della Terra, Universita degli Studi di Ancona, Ancona, Italy
SOURCE: Free Radical Biol. Med. (2000), 28(2), 193-201
CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We previously reported on the ability of dibenzoylmethane (DBM) and a relative, Parsol 1789, used as a UV A (UVA)-absorbing sunscreen, to generate free radicals upon illumination, and as a consequence, to inflict strand breaks in plasmid DNA in vitro. This study has now been extended to det. the effects of Parsol 1789 and DBM on proteins, under UVA illumination, with the sole purpose of gaining more knowledge on the photobiol. effects of sunscreen chems. Parsol 1789 (100 .mu.M) caused a 2-fold increase in protein carbonyl formation (an index of oxidative damage) in bovine serum albumin (BSA) when exposed to illumination, and this damage was both concn.- and time-dependent. The degree of protein damage was markedly reduced by the presence of free radical scavengers, namely piperidinic and indolinonic nitroxide radicals, in accordance with our previous study. Vitamin E had no effect under the conditions used. The results obtained corroborate the fact that Parsol 1789 generates free radicals upon illumination and that these are, most probably, responsible for the protein damage obsd. under the conditions used in our system. However, at present, we cannot extrapolate from these results the relevance to human use of sunscreens; therefore, further studies should be necessary to det. the efficacy at the mol. and cellular level of this UVA-absorber in order to ascertain protection against photocarcinogenic risk.
CC 8-9 (Radiation Biochemistry)
IT Carcinogens
(photo; sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)
IT **Albumins**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(serum; sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)
IT Antioxidants
Oxidative stress, biological
Sunscreens
UV A radiation
(sunscreen-induced **free radical** generation and

serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

IT Nitroxides
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

IT **Radicals**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

IT 120-46-7, Dibenzoylmethane 70356-09-1, Parsol 1789
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

IT 1406-18-4, Vitamin e 2226-96-2, Tempol 2564-83-2, Tempo 57309-27-0 57309-28-1 57309-32-7 57309-38-3
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

IT 50-01-1, Guanidine hydrochloride 119-26-6, 2,4-Dinitrophenylhydrazine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sunscreen-induced **free radical** generation and serum **albumin damage** by UVA illumination and antioxidant action of nitroxide **radicals**)

REFERENCE COUNT: 10
REFERENCE(S):
(1) Andrae, I; J Photochem Photobiol 1997, V37, P147 HCAPLUS
(3) Beckwith, A; J Am Chem Soc 1992, V114, P4983 HCAPLUS
(5) Chetelat, A; Mutat Res 1993, V292, P241 HCAPLUS
(8) Falcioni, G; Free Radic Res 1998, V28, P507 HCAPLUS
(9) Fuchs, J; Free Radic Biol Med 1998, V24, P643 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:600725 HCAPLUS
DOCUMENT NUMBER: 132:191265
TITLE: Development and application of novel biomarkers specific to **free radical** and lipid peroxidation modified proteins
AUTHOR(S): Osawa, Toshihiko
CORPORATE SOURCE: Nagoya University School of Bioagricultural Science, Nagoya, 464-8601, Japan
SOURCE: Furi Rajikaru no Rinsho (1998), 13, 8-13
CODEN: FRRIFI
PUBLISHER: Nihon Igakukan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 23 refs. Lipid peroxidn. is known to be a free radical chain reaction which takes place in vivo and in vitro and forms lipid hydroperoxides and secondary products. These lipid peroxidn. products are highly reactive and have been shown to interact with many biol. components

such as proteins, amino acids, amines, and DNA. Recently we have been involved in developing a novel type of evaluation systems for oxidative stress using immunochem. methods by application of polyclonal antibodies which are specific to 13-hydroperoxy linoleic acid (13-HPODE), malondialdehyde (MDA) and 4-hydroxy-4-nonenal (HNE), because immuno-chem. methods are specific, simple and convenient. We have also succeeded in developing a novel monoclonal antibody which are specific to HNE-modified BSA. We made an evaluation by monitoring the amt. of 8-OH-dG in biol. samples using the monoclonal antibody method, and succeeded in developing a new ELISA method in quantitating 8-OH-dG by competitive inhibition. These immunochem. methods for detection of lipid peroxidn. products and oxidatively damaged DNA are very specific and useful technique to investigate the lipid peroxidn. mechanism from the view point of mol. level. By application of the immunochem. technique to the antioxidative assay systems, we can make the reliable, simple and convenient evaluation methods of antioxidative substances.

CC 9-0 (Biochemical Methods)

IT Antioxidants
**Immunoassay**
Oxidative stress, biological
(development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Proteins, general, biological studies
**Radicals**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT **Immunoassay**
(enzyme-linked immunosorbent **assay**; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Lipids, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(hydroperoxides; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Peroxidation
(lipid; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Hydroperoxides
Peroxides, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(lipid; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Lipids, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(peroxides; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT Lipids, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(peroxidn.; development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

IT **Albumins**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serum, bovine; development and application of novel biomarkers specific to **free radical** and lipid peroxidn.

modified proteins)
IT 542-78-9, Malondialdehyde 23017-93-8 29343-52-0, 4-Hydroxy-2-nonenal 88847-89-6, 8-Hydroxy-2'-deoxy-guanosine
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(development and application of novel biomarkers specific to **free radical** and lipid peroxidn. modified proteins)

L25 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:558281 HCAPLUS
DOCUMENT NUMBER: 131:307072
TITLE: The Hydroxyl Free Radical Reactions of Ascorbyl Palmitate as Measured in Various in Vitro Models
AUTHOR(S): Perricone, N.; Nagy, K.; Horvath, F.; Dajko, G.; Uray, I.; Zs.-Nagy, I.
CORPORATE SOURCE: Department of Dermatology, Yale School of Medicine, New Haven, CT, USA
SOURCE: Biochem. Biophys. Res. Commun. (1999), 262(3), 661-665
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The OH.bul. free radical scavenging properties of ascorbyl palmitate (AP), water-solubilized in the presence of a surfactant (Brij 35), were tested in various systems: (1) The inhibition of polymn. of bovine serum albumin by OH.bul. free radicals generated by the Fenton reaction indicated AP exerts a considerable protective effect against polymn. by scavenging the OH.bul. free radicals. (2) ESR spin trapping comparisons of DMPO with AP were conducted. Using the Fenton reaction as a source of OH.bul. free radicals, AP was 1 order of magnitude faster in scavenging these radicals than DMPO. (3) Oxidative modification of BSA by 60Co-gamma irradn. of 80 krad, results in a strong increase in protein carbonyl content. AP inhibits carbonyl formation very efficiently, indicating that AP may be utilized as a biol. OH.bul. free radical scavenger in human therapy. (c) 1999 Academic Press.
CC 1-12 (Pharmacology)
IT Oxidation
(ascorbyl palmitate as **free radical** scavenger: .gamma.-ray-induced oxidative **damage** of **albumin**)
IT Gamma ray
(irradn.; ascorbyl palmitate as **free radical** scavenger: .gamma.-ray-induced oxidative **damage** of **albumin**)
REFERENCE COUNT: 32
REFERENCE(S):
(1) Aiedeh, K; J Microencapsul 1997, V14, P567 HCAPLUS
(2) Baader, W; Biochem Pharmacol 1988, V37, P1089 HCAPLUS
(3) Battalora, M; Carcinogenesis 1993, V14, P2507 HCAPLUS
(4) Bissett, D; Photodermatol Photoimmunol Photomed 1990, V7, P56 HCAPLUS
(5) Bruun-Jensen, L; Z Lebensm Untersuch Forsch 1994, V199, P210 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:200666 HCAPLUS
DOCUMENT NUMBER: 128:293113
TITLE: Chelating effect of human serum proteins on **metal**-catalyzed ascorbate radical generation

AUTHOR(S): Satoh, Kazue; Ida, Yoshiteru; Kimura, Satoshi; Taguchi, Kazumi; Numaguchi, Masahide; Gomi, Kunihide; Kochi, Mutsuyuki; Sakagami, Hiroshi
CORPORATE SOURCE: Analysis Center, School of Pharmaceutical Sciences, Showa University, Tokyo, 142, Japan
SOURCE: Anticancer Res. (1997), 17(6D), 4377-4380
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purified human serum albumin and IgG (IgG) were investigated for their metal-chelating activity, using ESR spectroscopy. Both copper (Cu2+) and iron ions (Fe3+) enhanced the radical intensity of both sodium ascorbate and sodium 5,6-benzylidene-L-ascorbate (SBA). Albumin significantly reduced the stimulation effect of copper, but not that of iron. On the other hand, IgG effectively reduced the radical intensity of iron, without affecting that of copper. The present study demonstrates the specific chelating action of these serum proteins, suggesting their possible preventive effects on metal-catalyzed pathogenic diseases.

CC 13-2 (Mammalian Biochemistry)

ST serum protein **metal** catalyzed ascorbate radical; iron copper chelation serum **albumin** IgG

IT Chelation
(chelating effect of human serum proteins on **metal**-catalyzed ascorbate radical generation)

IT IgG
Serum **albumin**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(chelating effect of human serum proteins on **metal**-catalyzed ascorbate radical generation)

IT 7439-89-6, Iron, biological studies 7440-50-8, Copper, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(chelating effect of human serum proteins on **metal**-catalyzed ascorbate radical generation)

IT 6730-29-6, L-Ascorbic acid, **free radical** from
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(chelating effect of human serum proteins on **metal**-catalyzed ascorbate **radical** generation)

L25 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:646338 HCAPLUS
DOCUMENT NUMBER: 121:246338
TITLE: Superoxide dismutase gene mutations as causes of neurodegenerative diseases and compounds and methods for the diagnosis, treatment, and prevention of the diseases
INVENTOR(S): Brown, Robert; Horvitz, H. Robert; Rosen, Daniel R.
PATENT ASSIGNEE(S): General Hospital Corp., USA; Massachusetts Institute of Technology
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| WO 9419493 | A1 | 19940901 | WO 1994-US2089 | 19940228 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5843641 | A | 19981201 | US 1993-23980 | 19930226 |
| CA 2157041 | AA | 19940901 | CA 1994-2157041 | 19940228 |
| EP 686203 | A1 | 19951213 | EP 1994-910183 | 19940228 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 08510377 | T2 | 19961105 | JP 1994-519309 | 19940228 |
| US 5849290 | A | 19981215 | US 1995-486953 | 19950607 |

PRIORITY APPLN. INFO.:
US 1993-23980 19930226
US 1994-204052 19940228
WO 1994-US2089 19940228

AB Disclosed is the family of genes responsible for the neurodegenerative diseases, particularly amyotrophic lateral sclerosis (ALS). Methods and compds. for the diagnosis, prevention, and therapy of the disease are also disclosed. Uses of the compds. in the prepn. of diagnostic and therapeutic medicaments are also provided. Fourteen different SOD1 missense mutations in 16 different familial ALS families were identified. The mutations were identified by PCR followed by single-strand conformational polymorphism anal. The most common single mutation was an Ala-4 to Val substitution in exon 1. This mutation reduced the total SOD activity by 50% compared to normal controls. Addnl. polymorphisms were identified in exons 3 and 4 as well as in intron 3. Some of these mutations are detectable by restriction fragment length polymorphism.

IC ICM C12Q001-68
ICS C12P019-34; C07H021-04

CC 1-11 (Pharmacology)
Section cross-reference(s): 3, 9, 14

IT **Antibodies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-SOD; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT Enzymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**free radical**-producing, inhibitors of; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT **Albumins**, biological studies
Ferritins
Lazaroids
**Metallothioneins**
Sulfonamides
Thiols, biological studies
Transferrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**metal**-binding, apo-; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis, treatment, and prevention of the diseases)

IT **Antibodies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, anti-SOD; superoxide dismutase gene mutations as causes of neurodegenerative diseases and compds. and methods for diagnosis,

treatment, and prevention of the diseases)

L25 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:418077 HCAPLUS
DOCUMENT NUMBER: 121:18077
TITLE: Radiopharmaceutical bacteriostats comprising benzalkonium and benzethorium chloride
INVENTOR(S): Tartaglia, Daniel; Flanagan, Richard J.
PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.
SOURCE: U.S., 18 pp. Cont.-in-part of U.S. 5,227,152.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5306482 | A | 19940426 | US 1992-841281 | 19920303 |
| US 5093105 | A | 19920303 | US 1991-682170 | 19910409 |
| US 5227152 | A | 19930713 | US 1991-806572 | 19911212 |
| CA 2065462 | AA | 19921010 | CA 1992-2065462 | 19920407 |
| EP 508724 | A1 | 19921014 | EP 1992-303074 | 19920407 |
| EP 508724 | B1 | 19960807 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE | | | | |
| AT 141059 | E | 19960815 | AT 1992-303074 | 19920407 |
| JP 05271102 | A2 | 19931019 | JP 1992-133069 | 19920409 |
| JP 07072144 | B4 | 19950802 | | |

PRIORITY APPLN. INFO.: US 1991-682170 19910409
US 1991-806572 19911212
US 1992-841281 19920303

AB Benzalkonium chloride (I) and benzethorium chloride are useful in radiopharmaceutical prepns. (optionally in the presence of a polymyxin or a polymyxin deriv.) as bacteriostatic agents which are compatible with anti-oxidants. A compn. contg. methylene diphosphonic acid 10, SnCl2.2H2O 1, PABA 2 mg, and I 50.mu.g was prepd. and lyophilized. The compn. was reconstituted with 500mCi 99Tc Na pertechnetate in 10mL water and left at room temp. for 24 h. The amt. of TcO4 in the soln. after this period was <1%.

IC ICM A61K043-00
ICS A61K049-02

NCL 424001370

CC 63-6 (Pharmaceuticals)

IT **Radicals**, biological studies
RL: BIOL (Biological study)
(**free**, scavengers of, radiopharmaceuticals contg. bacteriostats and)

IT **Antibodies**
RL: BIOL (Biological study)
(monoclonal, to fibrin and myosin, complexes with technetium 99-m, radiopharmaceuticals contg. benzalkonium and benzethorium chloride bacteriostats and)

IT **Albumins**, uses
RL: BIOL (Biological study)
(technetium complexes, labeled with technetium-99, radiopharmaceuticals contg. benzalkonium and benzethorium chloride bacteriostats and)

IT 14133-76-7DP, Technetium 99, complexes with **albumins**, preparation
RL: PREP (Preparation)
(metastable, radiopharmaceuticals contg. benzalkonium and benzethorium

chloride bacteriostats and)

L25 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:211487 HCAPLUS
DOCUMENT NUMBER: 118:211487
TITLE: A fluorescamine-based **assay** for the degree of glycation in bovine serum **albumin**
AUTHOR(S): Yaylayan, Varoujan A.; Huyghues-Despointes, Alexis; Polydorides, Angeliki
CORPORATE SOURCE: Dep. Food Sci. Agric. Chem., McGill Univ., Ste Anne de Bellevue, PQ, H9X 1C0, Can.
SOURCE: Food Res. Int. (1992), 25(4), 269-75
CODEN: FORIEU; ISSN: 0963-9969
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The fluorescence resulting from the reaction of a protein with fluorescamine is an indication of the no. of free amino groups in that protein, consequently glycated proteins which have fewer free amino groups will show less fluorescence. With the appropriate stds., the difference in fluorescence of glycated and non-glycated proteins can be translated into the no. of glycated sites in a protein. Glucose (0.22 M final concn.) was incubated with bovine serum albumin (BSA) (0.1 mg/mL) in a total vol. of 50 mL of 0.1 M phosphate buffer pH 7.2 at 37.degree. for a period of 35 days. To assess the effect of metal catalyzed free radical damage to the protein, the incubation was also carried out in the presence of a metal chelating agent EGTA (0.38 mg/mL). As expected, the fluorescence of both mixts. decreased with time, as more lysyl groups became glycated. Calcns. based on the std. curve of t-BOC-lysine showed that approx. 18 mol of glucose were incorporated per mol of BSA during the incubation in the presence of EGTA and 23 mol in the absence of EGTA. This difference is explained by the metal-catalyzed free radical fragmentation of BSA which exposes more N-terminal amino groups for reaction with glucose.
CC 17-1 (Food and Feed Chemistry)
ST **albumin** glycation assessment fluorescamine fluorescence
IT **Albumins**, analysis
RL: ANST (Analytical study)
(bovine, **assay** of degree of glycation of, fluorescamine fluorescence in)
IT Radical ions
(**metal** catalyzed formation of, bovine serum **albumin** fragmentation by, degree of glycation estn. from fluorescamine fluorescence in relation to)
IT Glycosidation
(glycation, of bovine serum **albumin**, fluorescamine fluorescence for **assay** for degree of)
IT Trace elements, miscellaneous
RL: MSC (Miscellaneous)
(**metals**, protein **free radical** **damage** catalyzed by, degree of glycation **assay** from fluorescamine fluorescence in relation to)
IT 38183-12-9, Fluorescamine
RL: ANST (Analytical study)
(bovine serum **albumin** interaction with, fluorescence from, degree of glycation estn. from)

L25 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:545016 HCAPLUS
DOCUMENT NUMBER: 117:145016
TITLE: Changes in **free radicals**, trace

elements, and neurophysiological function in rats with liver **damage** induced by D-galactosamine
AUTHOR(S): Hu, Henglong; Chen, Rendun
CORPORATE SOURCE: Dep. Nutr., Inst. Infect. Dis., Beijing, 100039, Peop. Rep. China
SOURCE: Biol. Trace Elem. Res. (1992), 34(1), 19-25
CODEN: BTERDG; ISSN: 0163-4984
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The changes in trace elements, free radicals, and neurophysiol. function were investigated in rats with liver damage induced by D-galactosamine (GalN). The elevated results showed that all the parameters related to free radical metab. changed after administration of GalN. Relative free radical concn., malonaldehyde (MDA), and GSSG elevated, but GSH decreased. Concurrently, zinc, copper, manganese, and selenium contents in liver were significantly reduced, whereas iron was elevated. In rats with hepatic encephalopathy (HE) owing to fulminant hepatic failure (FHF) induced by a high dosage of GalN, the latencies of visual evoked potentials (VEPs) were delayed. Moreover, there is a correlation between Zn content of brain and the latencies of VEPs. The results of this study suggested that lipid peroxidn. by free radicals might be responsible for GalN-induced liver damage in which trace elements were involved, and that change in brain Zn might play a role in the neural inhibition of HE owing to FHF.
CC 4-3 (Toxicology)
IT Liver, toxic chemical and physical **damage**
(galactosamine toxicity to, **free radicals** and trace elements and neurophysiol. during)
IT **Albumins**, biological studies
Prealbumins
RL: BIOL (Biological study)
(of tissue, galactosamine effect on, other tissues comparison with, hepatotoxicity in relation to)
IT Trace elements, biological studies
RL: BIOL (Biological study)
(heavy **metals**, in galactosamine toxicity to liver)
IT 7535-00-4, D-Galactosamine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to liver, **free radicals** and trace elements and neurophysiol. during)

L25 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:35817 HCAPLUS
DOCUMENT NUMBER: 116:35817
TITLE: **Radical**-induced **damage** to proteins: ESR spin-trapping studies
AUTHOR(S): Davies, Michael J.; Gilbert, Bruce C.; Haywood, Rachel M.
CORPORATE SOURCE: Dep. Chem., Univ. York, Heslington/York, YO1 5DD, UK
SOURCE: Free Radical Res. Commun. (1991), 15(2), 111-27
CODEN: FRRCEX; ISSN: 8755-0199
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reactions of hydroxyl radicals generated from Fe11/H2O2 and Cu11/H2O2 redox couples with a variety of proteins (bovine serum albumin, histones, cytochrome c, lysozyme and protamine) are investigated by ESR spin trapping. The signals obtained, which are generally anisotropic in nature, characterize the formation of partially immobilized spin-adducts resulting from attack of the HO.bul. radicals on the protein and subsequent reaction of the protein-derived radicals with the spin trap. Similar spin adducts are obsd. on incubation of two heme-proteins (Hb and

myoglobin) with H2O2 in the absence of added metal ions implying a reaction at the heme center followed by internal electron transfer reactions. Two strategies are employed to obtain information about the site(s) of radical damage in these proteins. The first involves the use of a variety of spin traps and in particular DMPO: with this particular trap the broad spectra from largely immobilized radicals show characteristic .alpha.(.beta.-H) values which enable carbon-, oxygen- and sulfur-centered radicals to be distinguished. The second involves the use of enzymic cleavage of first-formed adducts to release smaller nitroxides, with isotropic spectra, which allow the recognition of .beta.-proton splittings and hence information about the sites of radical damage to be obtained. These results, which allows backbone and side-chain attack to be distinguished, are in agreement with random attack of the HO.bul. radical on the protein and are in accord with studies carried out on model peptides. In contrast the use of less reactive attacking radicals [N3.bul.,.bul.CH(CH3)OH] and oxidizing agents (Ce41) provides evidence for selective attack on these proteins at particular residues.

CC 4-3 (Toxicology)
Section cross-reference(s): 6

ST **radical** protein **damage**; hydroxyl **radical** protein **damage**; hydrogen peroxide **metal** protein oxidn; oxidative **damage radical** protein

IT Histones
RL: BIOL (Biological study)
(2S, hydroxyl **radical**-induced **damage** of, after reaction with hydrogen peroxide and **metal**, ESR in studies of)

IT Oxidative stress, biological
(hydrogen peroxide and **metal** mediation of, protein damage induction by, ESR in studies of)

IT **Albumins**, biological studies
Hemoglobins, met-
Myoglobins
Protamines
RL: BIOL (Biological study)
(hydroxyl **radical**-induced **damage** of, after reaction with hydrogen peroxide and **metal**, ESR in studies of)

IT **Radicals**, biological studies
RL: BIOL (Biological study)
(protein **damage** induction by, ESR in studies of)

IT Proteins, biological studies
RL: BIOL (Biological study)
(**radical**-induced **damage** of, ESR in studies of)

IT Histones
RL: BIOL (Biological study)
(H2A, hydroxyl **radical**-induced **damage** of, after reaction with hydrogen peroxide and **metal**, ESR in studies of)

IT 3695-73-6 5874-90-8 7093-67-6 17123-30-7 19729-30-7 24991-23-9 25513-46-6, Polyglutamic acid 25608-40-6, Polyaspartic acid 26063-13-8, Polyaspartic acid 26894-34-8, Polyasparagine 28088-48-4, Polyasparagine 70195-20-9
RL: BIOL (Biological study)
(hydroxyl **radical** reaction with, ESR in studies of, **radical**-induced **damage** of proteins in relation to)

IT 56-86-0, L-Glutamic acid, properties 56-87-1, L-Lysine, properties 59-51-8, DL-Methionine 63-91-2, L-Phenylalanine, properties 73-22-3, L-Tryptophan, properties 74-79-3, L-Arginine, properties 302-72-7, DL-Alanine 328-39-2, DL-Leucine 556-33-2 556-50-3 637-84-3 687-69-4 837-83-2 926-79-4
RL: PRP (Properties)
(hydroxyl **radical** reaction with, ESR in studies of,

**radical**-induced **damage** of proteins in relation to)
IT 9001-63-2, Lysozyme 9007-43-6, Cytochrome c, biological studies
RL: BIOL (Biological study)
(hydroxyl **radical**-induced **damage** of, after reaction with hydrogen peroxide and **metal**, ESR in studies of)
IT 2348-46-1 12596-60-0, biological studies
RL: BIOL (Biological study)
(lysozyme **damage** induction by, **radical**-induced **damage** of proteins in relation to)
IT 7440-50-8, Copper, biological studies 15651-72-6
RL: BIOL (Biological study)
(protein **damage** induction by hydrogen peroxide and, hydroxyl **radical** mediation of, ESR in studies of)
IT 7722-84-1, Hydrogen peroxide (H2O2), biological studies
RL: BIOL (Biological study)
(protein **damage** induction by iron and copper and, hydroxyl **radical** mediation of, ESR in studies of)
IT 3352-57-6, Hydroxyl **radical**, biological studies
RL: BIOL (Biological study)
(protein **damage** induction by, ESR in studies of)
IT 7440-45-1, Cerium, reactions
RL: RCT (Reactant)
(reaction of, with **albumin**, ESR in studies of, **radical**-induced **damage** of proteins in relation to)

L25 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:1867 HCAPLUS
DOCUMENT NUMBER: 116:1867
TITLE: Free radical damage to proteins: the influence of the relative localization of radical generation, antioxidants, and target proteins
AUTHOR(S): Dean, Roger T.; Hunt, James V.; Grant, Adrienne J.; Yamamoto, Yorihiro; Niki, Etsuo
CORPORATE SOURCE: Heart Res. Inst., Sydney, 2050, Australia
SOURCE: Free Radical Biol. Med. (1991), 11(2), 161-8
CODEN: FRBMEH; ISSN: 0891-5849
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Free radicals were generated at known rates in the aq. phase (by means of 2,2'-azobis (2-amidinopropane) dihydrochloride [AAPH]) and a membranous (lipid) phase (by means of 2,2'-azobis (2,4-dimethylvaleronitrile [AMVN]). A sol. protein (bovine serum albumin: BSA), and membranes of lysed mitochondria contg. radioactively labeled monoamine oxidase (MAO), were exposed to the resultant radical fluxes. Antioxidants were added to the system, either in the aq. phase (Trolox) or in a liposomal membrane phase (.alpha.-tocopherol). Protein damage was assessed as tryptophan oxidn. and conformational changes in tryptophan fluorescence of the sol. protein BSA, and as fragmentation of both BSA and monoamine oxidase. Radicals generated in the aq. phase, by AAPH, were effective in damaging BSA and MAO. Radicals generated within the liposome membrane phase (by AMVN) were less effective against BSA than those deriving from AAPH. Liposomal AMVN radicals could damage MAO, present in a sep. membranous phase, though again, less effectively than could AAPH-derived radicals. BSA could be protected by Trolox, the aq. sol. antioxidant, but hardly by tocopherol itself. Damage to MAO was limited by Trolox, and also by the hydrophobic antioxidant, tocopherol. Damaging reactions due to radicals generated in a membrane phase were significantly accelerated when the membrane was peroxidizable (soybean phosphatidylcholine) rather than nonperoxidizable (satd. dimyristoyl phosphatidylcholine). Thus, lipid radicals also played some role in protein damage in these systems. BSA was attacked similarly

in the presence or absence of liposomes by AAPH. Correspondingly, BSA could inhibit the peroxidn. of liposomes induced by AAPH and less efficiently that induced by AMVN. Evidently, the relative localization of radical generation, antioxidants, and protein targets has a major influence on the extent of radical attack on proteins and membranes.

CC 4-3 (Toxicology)

IT **Albumins**, biological studies
RL: BIOL (Biological study)
(**free radical damage** of)

L25 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:527570 HCAPLUS
DOCUMENT NUMBER: 115:127570
TITLE: **Free radical**-induced carbonyl content in protein of estrogen-treated hamsters **assayed** by sodium boro[3H]hydride reduction
AUTHOR(S): Winter, Mark L.; Liehr, Joachim G.
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Texas, Galveston, TX, 77550-2774, USA
SOURCE: J. Biol. Chem. (1991), 266(22), 14446-50
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oxidn. damage to proteins is known to occur via conversion of side chain amino groups to corresponding carbonyl derivs. Such damage to enzymes and purified proteins has been quantified previously by redn. with sodium boro[3H]hydride and subsequent measurement of the incorporation of 3H into amino acid fractions. In this study, the NaB3H4 redn. assay was modified to permit the quantitation of free radical-mediated oxidative damage to proteins obtained from animals. Modifications included addnl. extns. of protein isolates with org. solvents to remove lipids and with nitric acid to remove metal ions. The modified assay has first been validated in vitro by measuring changes in levels of oxidative damage to bovine serum albumin exposed to xanthine plus xanthine oxidase (2-fold increase), to hydrogen peroxide and iron(II) sulfate (5-fold increase), or to .gamma. radiation (30-fold increase over controls, resp.). .gamma. Radiation of isolated hamster kidney protein also raised the carbonyl content in a dose-dependent manner. The modified assay has been been validated in vivo by measuring the changes in oxidative damage to lung tissue in animals exposed to .apprx.85% oxygen (2-fold increase) or to different doses of paraquat (5-fold increases with the high dose over controls, resp.). The assay was then used to examine free radical-mediated oxidn. introduced by acute or chronic treatment of hamsters with estrogens, since both synthetic and natural estrogens induce kidney tumors in this species. Priming of hamsters for 3 days with 20 mg/kg/day diethylstilbestrol and treatment with 100 mg/kg of this drug on the 4th day resulted in a 160% increase in free radical modification of renal proteins. Oxidative damage to kidney proteins was also assayed in hamsters treated with estradiol implants for <7 mo, a regimen known to induce kidney tumors. Significant increases in covalent oxidative modification to renal proteins over values in age-matched controls were detected after 1, 2, and 7 mo of continuous estradiol exposure. Thus, the modification of the NaB3H4 redn. assay is a useful postlabeling method for monitoring free radical action in vivo. Furthermore, it is postulated that free radical damage in estrogen-treated hamster kidney plays a role in estrogen-induced carcinogenesis.

CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 4, 8, 9, 14

ST estrogen protein **damage** kidney carcinogenesis; **free radical** carbonyl protein **damage**; sodium borohydride protein **damage** detn

IT Proteins, biological studies
RL: BIOL (Biological study)
(estrogen-induced damage of, of kidney, carbonyl detn. by borohydride redn. in **assay** of)
IT Kidney, toxic chemical and physical damage
(from estrogens, preradicals in, carbonyl detn. in protein by borohydride redn. in **assay** of)
IT Lung, toxic chemical and physical damage
(from hyperoxia and paraquat, carbonyl detn. in protein by borohydride redn. **assay** of)
IT **Radicals**, biological studies
RL: BIOL (Biological study)
(in estrogen-induced kidney oxidative **damage**)
IT Gamma ray, biological effects
(kidney protein oxidative damage from, carbonyl detn. by borohydride redn. in **assay** of)
IT Hyperoxia
(long oxidative damage from, protein carbonyl detn. by borohydride redn. in **assay** of)
IT 7720-78-7, Iron(II) sulfate
RL: BIOL (Biological study)
(**albumin** oxidative damage from hydrogen peroxide and, carbonyl detn. by borohydride redn. in **assay** of)
IT 7722-84-1, Hydrogen peroxide, biological studies
RL: BIOL (Biological study)
(**albumin** oxidative damage from iron sulfate and, carbonyl detn. by borohydrate redn. in **assay** of)
IT 9002-17-9, Xanthine oxidase
RL: BIOL (Biological study)
(**albumin** oxidative damage from xanthine and, carbonyl content detn. by borohydride redn. in **assay** of)
IT 69-89-6, Xanthine
RL: BIOL (Biological study)
(**albumin** oxidative damage from xanthine oxidase and, carbonyl content detn. by borohydrate redn. in **assay** of)
IT 4685-14-7, Paraquat
RL: BIOL (Biological study)
(long oxidative damage from, protein carbonyl detn. by borohydride redn. in **assay** of)

L25 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:422201 HCAPLUS
DOCUMENT NUMBER: 115:22201
TITLE: Superoxide dismutase-catalase conjugates as tissue-specific therapeutics
INVENTOR(S): Poznansky, Mark J.; Mao, Guo Dong
PATENT ASSIGNEE(S): University of Alberta, Can.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9103548 | A1 | 19910321 | WO 1990-CA279 | 19900830 |
| W: AU, CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE | | | | |
| CA 2065430 | AA | 19910301 | CA 1990-2065430 | 19900830 |

| | | | | |
|---|---|---|---|---|
| AU 9062854 | A1 | 19910408 | AU 1990-62854 | 19900830 |
| US 5336493 | A | 19940809 | US 1992-836274 | 19920302 |
| PRIORITY APPLN. INFO.: | | | GB 1989-19661 | 19890831 |
| | | | WO 1990-CA279 | 19900830 |

AB A novel multicomponent conjugate having superoxide dismutase (SOD), catalase, and optionally albumin and a targeting agent such as antibody is provided. A pharmaceutical compn. contg. such conjugate can be used for tissue-specific scavenging of superoxide and hydroxyl radicals with higher efficiency than SOD or catalase alone. The half-life of the SOD-catalase conjugates was 300 min in rats. Scavenging of the free radicals using the conjugates was also demonstrated in vitro and in the rat heart model of ischemia-reperfusion.

IC ICM C12N009-96

CC 1-4 (Pharmacology)

IT **Antibodies**
RL: BIOL (Biological study)
(conjugates with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl **free radicals**
)

IT Myosins
RL: BIOL (Biological study)
(monoclonal **antibody** to, conjugates with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl radicals)

IT **Albumins**, compounds
RL: BIOL (Biological study)
(conjugates, with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl radicals)

IT **Antibodies**
RL: BIOL (Biological study)
(monoclonal, conjugates with superoxide dismutase and catalase, for tissue-specific scavenging of superoxide and hydroxyl **free radicals**)

IT 9001-05-2DP, Catalase, conjugates with superoxide dismutase 9054-89-1DP, Superoxide dismutase, conjugates with catalase
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for superoxide and hydroxyl **free radical** scavenging)

L25 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2001 ACS

| | |
|---|---|
| ACCESSION NUMBER: | 1991:201358 HCAPLUS |
| DOCUMENT NUMBER: | 114:201358 |
| TITLE: | Stimulatory and inhibitory actions of proteins and amino acids on copper-catalyzed **free radical** generation in the bulk phase |
| AUTHOR(S): | Simpson, Jeremy A.; Dean, Roger T. |
| CORPORATE SOURCE: | Heart Res. Inst., Sydney, 2050, Australia |
| SOURCE: | Free Radical Res. Commun. (1990), 10(4-5), 303-12 CODEN: FRRCEX; ISSN: 8755-0199 |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

AB The effect of a variety of proteins and amino acids was investigated on oxygen free radical activity as assessed by copper/hydrogen peroxide induced benzoate hydroxylation as well as copper-catalyzed ascorbate autoxidn. Serum albumins from a variety of species (human, bovine, and dog) had both inhibitory and stimulatory effects depending on the molar copper to protein ratio; low ratios were inhibitory and high stimulatory. Some other proteins tested (lysozyme, soybean trypsin inhibitor, and conalbumin) also had dual (inhibitory and stimulatory) effects, as did both histidine and polyhistidine, but all effects occurred at different

molar ratios presumably dependent on the relative affinities for the copper ions. In contrast, metallothionein and ceruloplasmin, proteins specialized to bind copper in vivo, had no stimulatory effects. In addn. to their fairly well documented inhibitory effects, under certain conditions some proteins also stimulate radical reactions. The possible role of this phenomenon in vivo is discussed.

CC 4-3 (Toxicology)

ST protein amino acid copper **free radical**

IT **Albumins**, biological studies
Amino acids, biological studies
**Metallothioneins**
Proteins, biological studies
RL: BIOL (Biological study)
(copper-catalyzed **free radical** generation response to)

IT 71-00-1, Histidine, biological studies 1391-06-6, Conalbumin 9001-63-2, Lysozyme 9031-37-2, Ceruloplasmin 9078-38-0 26062-48-6, Polyhistidine 26854-81-9, Polyhistidine
RL: BIOL (Biological study)
(copper-catalyzed **free radical** generation response to)

IT 7440-50-8, Copper, biological studies
RL: BIOL (Biological study)
(**free radical** generation catalyzed by, proteins and amino acids effect on)

L25 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:141132 HCAPLUS

DOCUMENT NUMBER: 114:141132

TITLE: Characterization of a monoclonal **antibody** to thymidine glycol monophosphate

AUTHOR(S): Chen, Bi Xing; Hubbard, Karen; Ide, Hiroshi; Wallace, Susan S.; Erlanger, Bernard F.

CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA

SOURCE: Radiat. Res. (1990), 124(2), 131-6
CODEN: RAREAE; ISSN: 0033-7587

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoclonal antibody specific for thymine glycol (TG) in irradiated or OsO4-treated DNA was obtained by immunizing with thymidine glycol monophosphate (TMP-glycol) conjugated to bovine serum albumin by a carbodiimide procedure. Screening by dot-immunobinding and ELISA procedures gave 9 clones that bound OsO4-treated DNA. One of them, 2.6F.6B.6C, an IgG2a.kappa., was characterized further. Hapten inhibition studies with OsO4-treated DNA showed that the antibody was specific for TMP-glycol. Among the various inhibitors tested, inhibition was in the order TMP-glycol > 5,6-dihydrothymidine phosphate > TMP > thymidine glycol > TG. Inhibition by 5,6-dihydrothymidine, thymidine, thymine, AMP, and CMP was negligible. In OsO4-treated DNA, as few as 0.5 TG per 10,000 bp were detectable by direct ELISA. Inhibition assays could detect as few as 1.5 TG per 10,000 bp. The antibody was equally reactive with native or denatured DNA contg. TG. Among the X-irradiated homopolymers dC, dA, dG, and dT, only dT reacted with the antibody. Using an ELISA, the antibody could detect damage in irradiated DNA at the level of 20 Gy. Thus the antibody is of potential use in assays for DNA damage caused by X rays or other agents that damage DNA by free radical interactions.

CC 15-3 (Immunochemistry)
Section cross-reference(s): 8

ST monoclonal **antibody** thymidine glycol monophosphate

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(**damage** to, from X-ray or **free radicals**, monoclonal **antibody** to thymidine glycol monophosphate in relation to)
IT **Albumins**, compounds
RL: PREP (Preparation)
(conjugates, with thymidine glycol monophosphate, monoclonal **antibody** to, prepn. and characterization of)
IT **Antibodies**
RL: PREP (Preparation)
(monoclonal, to thymidine glycol monophosphate, prepn. and characterization of)
IT 365-07-1, Thymidine monophosphate 2943-56-8, Thymine glycol 32645-65-1, Thymidine glycol 69321-99-9
RL: BIOL (Biological study)
(**antibody** to thymidine glycol monophosphate cross-reactivity with)
IT 25086-81-1
RL: BIOL (Biological study)
(**antibody** to thymidine glycol monophosphate cross-reactivity with irradiated)
IT 6168-31-6D, **albumin** conjugates
RL: BIOL (Biological study)
(monoclonal **antibody** to, prepn. and characterization of)

L25 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:94805 HCAPLUS
DOCUMENT NUMBER: 114:94805
TITLE: Antiinflammatory reactivity of copper(I)-thionein
AUTHOR(S): Miesel, Ralf; Hartmann, Hans Juergen; Weser, Ulrich
CORPORATE SOURCE: Physiol.-Chem. Inst., Univ. Tuebingen, Tuebingen, 7400, Fed. Rep. Ger.
SOURCE: Inflammation (N. Y.) (1990), 14(5), 471-83
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In unseparated human blood the reactivity of yeast copper (I)-thionein on TPA-activated polymorphonuclear leukocytes was evaluated and compared with low-mol.-wt. Cu chelates exerting Cu, Zn-activated superoxide dismutase mimetic activity. Cu, 18 .mu.M, in the form of Cu-thionein was sufficient to inhibit the superoxide prodn. of activated human blood phagocytes by 50%. Furthermore, the scavenging of hydroxyl radicals and singlet oxygen by Cu(I)-thionein was detd., using the 2-deoxyribose fragmentation assay induced by decaying K3CrO8 and the NADPH oxidn. caused by UVA illuminated psoralen, resp. The inhibitory reactivity of Cu-thionein in both assays was compared with that of serum proteins including albumin, ceruloplasmin, transferrin, and ferritin. The galactosamine/endotoxin-induced hepatitis in male NMRI mice was used to evaluate the antiinflammatory reactivity of Cu-thionein in vivo. The serum Cu, superoxide dismutase, and sorbitol dehydrogenase concns., as well as the activity of polymorphonuclear leukocytes in unseparated blood seemed most appropriate to quantify the protective capacity of Cu-thionein in the course of an oxidative stress-dependent liver injury. The i.p. application of 32.5 .mu.mol/kg thionein-Cu limited this damage to 45%.
CC 1-7 (Pharmacology)
IT Phagocyte
(oxygen **free radicals** formation by human, copper thionein inhibition of, anti-inflammatory mechanism in relation to)
IT **Albumins**, biological studies

Ferritins
Transferrins
RL: BIOL (Biological study)
(scavenging of oxygen radicals in human phagocyte by copper thionein vs.)
IT **Metallothioneins**
RL: PRP (Properties)
(copper-contg., anti-inflammatory mechanism of)
IT Leukocyte
(polymorphonuclear, oxygen **free radicals** formation by human, copper thionein inhibition of, anti-inflammatory mechanism in relation to)

L25 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:167750 HCAPLUS
DOCUMENT NUMBER: 110:167750
TITLE: Phycoerythrin fluorescence-based **assay** for peroxy radicals: a screen for biologically relevant protective agents
AUTHOR(S): DeLange, Robert J.; Glazer, Alexander N.
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Anal. Biochem. (1989), 177(2), 300-6
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Under the conditions of this assay, antioxidants that react rapidly with peroxy free radicals (e.g., ascorbate, vitamin E analogs, and urate), protect phycoerythrin completely from damage by such radicals generated by thermal decompn. of 2,2'-azobis[(2-amidinopropane)]; other compds. provide partial concn.-dependent protection. Change in phycoerythrin fluorescence emission with time provides a measure of the rate of free radical damage. The assay exploits the unusual reactivity of phycoerythrin toward these peroxy radicals. On a molar basis, phycoerythrin reacts with these radicals >100-fold slower than do ascorbate or vitamin E analogs, but >60-fold faster than other proteins. Applications of this assay to the estn. of the peroxy radical scavenging capacity of human plasma are described, and to the comparison of the scavenging properties of several proteins and of DNA, of vitamins and their derivs., of catecholamine neurotransmitters, and of a variety of other low-mol.-wt. biol. compds.
CC 4-3 (Toxicology)
IT Blood plasma
(oxygen **radical damage** to phycoerythrin in, of humans, protective agent screening in relation to)
IT Antioxidants
Vitamins
RL: BIOL (Biological study)
(oxygen **radical damage** to phycoerythrin protection by, in human plasma, structure in relation to)
IT **Albumins**, biological studies
Deoxyribonucleic acids
Ovalbumins
Proteins, biological studies
RL: BIOL (Biological study)
(oxygen **radical damage** to phycoerythrin response to, in humans)
IT Named reagents and solutions
RL: BIOL (Biological study)
(Dulbecco's modified Eagle's, oxygen **radical damage** to phycoerythrin protection by, in human plasma, structure in relation

to)
IT Neurohormones
RL: BIOL (Biological study)
(neurotransmitters, oxygen **radical damage** to phycoerythrin protection by, in human plasma, structure in relation to)
IT Molecular structure-biological activity relationship
(oxygen radical formation-inhibiting, of protective agents, screening **assay** for)
IT Phycoerythrins
RL: BIOL (Biological study)
(B-, oxygen **radical damage** to, in human plasma, protective agent screening in relation to)
IT 50-67-9, Serotonin, biological studies 50-81-7, L-Ascorbic acid, biological studies 50-99-7, Glucose, biological studies 51-41-2, Norepinephrine 51-43-4, Epinephrine 51-45-6, Histamine, biological studies 51-61-6, Dopamine, biological studies 53-57-6, NADPH 53-59-8, NADP+ 59-43-8, Thiamine, biological studies 59-67-6, Nicotinic acid, biological studies 59-92-7, biological studies 63-68-3, Methionine, biological studies 69-93-2, biological studies 71-44-3, Spermine 85-61-0, Coenzyme A, biological studies 85-87-0, Pyridoxamine 110-60-1, Putrescine 121-44-8, Triethylamine, biological studies 146-17-8, Riboflavin 5'-(dihydrogen phosphate) 306-08-1 541-15-1, Carnitine 7365-45-9, HEPES 56305-04-5, Trolox
RL: BIOL (Biological study)
(oxygen **radical damage** to phycoerythrin protection by, in human plasma, structure in relation to)
IT 9001-63-2, Lysozyme
RL: BIOL (Biological study)
(oxygen **radical damage** to phycoerythrin response to, in humans)
IT 7782-44-7D, Oxygen, **radicals**
RL: BIOL (Biological study)
(phycoerythrin **damage** by, in human plasma, protective agent screening in relation to)

L25 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:107680 HCAPLUS
DOCUMENT NUMBER: 110:107680
TITLE: Oxidative damage to DNA and deoxyribose by .beta.-lactam antibiotics in the presence of iron and copper salts
AUTHOR(S): Quinlan, Gregory J.; Gutteridge, John M. C.
CORPORATE SOURCE: Div. Chem., Natl. Inst. Biol. Stand. Control, Potters Bar/Herts., EN6 3QG, UK
SOURCE: Free Radical Res. Commun. (1988), 5(3), 149-58
CODEN: FRRCEX; ISSN: 8755-0199
DOCUMENT TYPE: Journal
LANGUAGE: English
AB .beta.-Lactam antibiotics in the presence of certain metal ions damage deoxyribose and DNA with the release of thiobarbituric acid-reactive material. This damage can be substantially prevented by catalase, metal chelators and some scavengers of the hydroxyl radical. Ferric salts in the presence of certain .beta.-lactam antibiotics were effective in degrading deoxyribose but they did not appear to damage DNA. In contrast copper salts and .beta.-lactam antibiotics were extremely effective in damaging both DNA and deoxyribose.
CC 1-5 (Pharmacology)
IT **Albumins**, biological studies
RL: BIOL (Biological study)
(oxidative damage to deoxyribose and DNA by .beta.-lactam antibiotics

in presence of **metal** salts response to)
IT 7782-44-7D, Oxygen, **radicals**
RL: BIOL (Biological study)
(deoxyribose and DNA **damage** from .beta.-lactam antibiotics in presence of **metal** salts)
IT 57-13-6, Urea, biological studies 62-56-6, Thiourea, biological studies 64-18-6, Formic acid, biological studies 65-85-0, Benzoic acid, biological studies 69-65-8, Mannitol 70-51-9, Desferrioxamine 9001-05-2, Catalase 9054-89-1, Superoxide dismutase
RL: BIOL (Biological study)
(oxidative damage to deoxyribose and DNA by .beta.-lactam antibiotics in presence of **metal** salts response to)

L25 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:508420 HCAPLUS
DOCUMENT NUMBER: 109:108420
TITLE: Gastric mucosal lesions induced by hemorrhagic shock in baboons. Role of oxygen-derived free radicals
AUTHOR(S): Von Ritter, C.; Hinder, R. A.; Oosthuizen, M. M. J.; Svensson, L. G.; Hunter, S. J. S.; Lambrecht, H.
CORPORATE SOURCE: Dep. Surg., Univ. Witwatersrand, Johannesburg, S. Afr.
SOURCE: Dig. Dis. Sci. (1988), 33(7), 857-64
CODEN: DDSCDJ; ISSN: 0163-2116
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of oxygen-derived free radicals during ischemia and reperfusion in the prodn. of acute damage to the gastric mucosa of baboons was examd. The protective effect of the xanthine oxidase inhibitor, allopurinol, the superoxide scavenger, superoxide dismutase (SOD), and a long-acting SOD-albumin was detd. A similar pattern of tissue damage was found at the end of ischemia in all three (allopurinol + SOD, SOD-albumin, and control) groups. Thirty minutes after reperfusion, severe mucosal damage (grade 3) increased only in the untreated control. In the two treated groups, grade 3 damage remained unchanged during reperfusion and a decrease in the percentage of moderate damage (grade 2) was seen. Both GSH and GSSG tissue concns. were lower in the untreated controls as compared to the scavenger-treated groups, making it questionable whether GSH/GSSG tissue levels adequately reflect oxidative stress. Thus, the generation of oxygen-derived free radicals produces mucosal damage and prevents the restitution of moderate mucosal damage during reperfusion. In ischemia, factors other than free radicals seem to be responsible for mucosal damage. The protective effect of allopurinol and SOD was not mediated by changes in gastric mucosal blood flow.
CC 14-7 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1
IT Ischemia
(oxygen-derived **free radicals** mediation of **damage** during and after, in stomach, superoxide dismutase-**albumin** conjugate therapy in relation to)

L25 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:472274 HCAPLUS
DOCUMENT NUMBER: 107:72274
TITLE: Effect of **free radical** scavengers and **metal** ion chelators on hydrogen peroxide and phenylhydrazine induced red blood cell lipid peroxidation
AUTHOR(S): Einsele, Hermann; Clemens, Michael R.; Wegner, Ulrike; Waller, Hans Dierck
CORPORATE SOURCE: Med. Klin., Eberhard Karls Univ. Tuebingen, Tuebingen,

D-7400, Fed. Rep. Ger.
SOURCE: Free Radical Res. Commun. (1987), 3(1-5), 257-63
CODEN: FRRCEX; ISSN: 8755-0199
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Desferrioxamine a well-known Fe chelator decreased H2O2- and phenylhydrazine-induced lipid peroxidn. of red blood cell membranes assessed by hydrocarbon gas release and loss of polyunsatd. fatty acids. The OH scavengers like mannitol and thiourea and proteins like albumin were unable to reduce peroxidative reactions. Addn. of uric acid (in an unphysiol. concn. of 5 mM) to the incubation medium resulted in a slight redn. in H2O2/phenylhydrazine mediated break-down of arachidonic (20:4) and docosahexenoic acid (22:6) in the erythrocyte membrane and consequently in a decreased alkane release and hemolysis.
CC 4-3 (Toxicology)
IT **Albumins**, biological studies
RL: BIOL (Biological study)
(**free radical** induction of lipid peroxidn. response to, **radicals** scavengers in relation to)
IT Erythrocyte
(lipid peroxidn. in, by **free radicals**, **radical** scavengers effect on)
IT Peroxidation
(of lipids, hydrogen peroxide and phenylhydrazine induction by, in erythrocyte, **free radicals** scavengers effect on)
IT Lipids, biological studies
RL: BIOL (Biological study)
(peroxidn. of, hydrogen peroxide and phenylhydrazine induction of, in erythrocyte, **free radical** scavenger effect on)
IT 62-56-6, Thiourea, biological studies 64-17-5, Ethanol, biological studies 69-65-8, Mannitol 69-93-2, Uric acid, biological studies
RL: BIOL (Biological study)
(**free radical** induction of lipid peroxidn. response to, **radicals** scavengers in relation to)
IT 100-63-0, Phenylhydrazine
RL: BIOL (Biological study)
(lipid peroxidn. by, in erythrocyte, **free radicals** scavengers effect on)
IT 7722-84-1, Hydrogen peroxide, biological studies
RL: BIOL (Biological study)
(lipid peroxidn. induction by, in erythrocyte, **free radicals** scavengers effect on)

L25 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:223142 HCAPLUS
DOCUMENT NUMBER: 104:223142
TITLE: Role of some **free radicals** (sulfhydryl groups) in immune reactions and barrier function of spermatozoa membrane
AUTHOR(S): Kolinkoeva, A.
CORPORATE SOURCE: Inst. Biol. Immunol. Reprod. Dev. Org., Sofia, 1113, Bulg.
SOURCE: Dokl. Bolg. Akad. Nauk (1986), 39(2), 129-32
CODEN: DBANAD; ISSN: 0366-8681
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role and significance of SH groups, autoxidants, and other physiol.-active substances in antigen-antibody reactions was studied. Reactions among spermatozoa and antispermatozoal serum were used as a model system. Cysteine, serine, and dehydrocortisone enhanced the immune

reactions, but albumin, cholesterol, .alpha.-tocopherol, and .beta.-carotene suppressed the immune reactions.
CC 15-3 (Immunochemistry)
ST **antibody** antigen interaction sulfhydryl
IT **Albumins**, blood serum
RL: BIOL (Biological study)
(**antibody**-antigen reactions inhibition by)
IT **Antibodies**
RL: BIOL (Biological study)
(antigen reactivity with, sulfhydryl groups role in and autoxidants effect on)
IT Immunosuppressants
(autoxidants as, of **antibody**-antigen interactions)
IT Mercapto group
(in **antibody**-antigen reactions)
IT 52-90-4, biological studies 56-45-1, biological studies
RL: BIOL (Biological study)
(**antibody**-antigen interaction response to)
IT 16574-04-2
RL: BIOL (Biological study)
(**antibody**-antigen interaction stimulation by)
IT 57-88-5, biological studies 59-02-9 7235-40-7
RL: BIOL (Biological study)
(**antibody**-antigen interactions inhibition by)

L25 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:199930 HCAPLUS
DOCUMENT NUMBER: 102:199930
TITLE: Age pigments and **free radicals**: fluorescent lipid complexes formed by iron- and copper-containing proteins
AUTHOR(S): Gutteridge, John M. C.
CORPORATE SOURCE: Div. Antibiot. Chem., Natl. Inst. Biol. Stand. Control, Hempstead/London, NW3 6RB, UK
SOURCE: Biochim. Biophys. Acta (1985), 834(2), 144-8
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Heme and non-heme Fe-contg. proteins stimulate lipid peroxidn. with the formation of fluorescent lipid complexes. This process requires the presence of lipid hydroperoxides which release ferrozine-reactive Fe from heme-contg. proteins. Stimulation of lipid peroxidn. by the released Fe is inhibited by the Fe chelator desferrioxamine. Cu2+, although more stimulatory towards fluorescent lipid complex formation than Fe2+, does not stimulate lipid peroxidn. when tightly bound at the active center of proteins, but is reactive when loosely bound to albumin and histidine.
CC 6-5 (General Biochemistry)
Section cross-reference(s): 13
ST age pigment lipid peroxidn **metalloprotein**; copper protein lipid peroxidn age pigment; iron protein lipid peroxidn age pigment; radical lipid age pigment **metalloprotein**
IT **Albumins**, blood
RL: BIOL (Biological study)
(copper complexes, lipid peroxidn. stimulation by, age pigment formation in)

L25 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1976:587540 HCAPLUS
DOCUMENT NUMBER: 85:187540
TITLE: Spin labeled compounds for use in forensic analysis

INVENTOR(S): Goldstein, Avram; Leute, Richard K.; Ullman, Edwin F.
PATENT ASSIGNEE(S): Syva Co., USA
SOURCE: U.S., 46 pp. Continuation of U.S. 3,853,914.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3966744 | A | 19760629 | US 1974-482542 | 19740624 |
| US 3690834 | A | 19720912 | US 1971-141516 | 19710510 |
| FR 2121723 | A5 | 19720825 | FR 1972-687 | 19720110 |
| FR 2121723 | B1 | 19730629 | | |
| US 3853914 | A | 19741210 | US 1972-270108 | 19720710 |

PRIORITY APPLN. INFO.: US 1971-105535 19710111
US 1971-141516 19710510
US 1972-270108 19720710

AB Spin labeled compds. (ligand analogs) for use in forensic immunoassay were prepd. by modifying biol. active compds. or structural analogs and coupling them with a stable free radical compd. The ligand analog is recognizable by receptor mol., usually on antibody, and can compete with a biol. active mol. (ligand) for the receptor site in a way which allows the biol. active mol. to be assayed spectrometrically. For example, 2 mmoles amphetamine (I) [300-62-9] in 20 ml MeOH was treated with 106 mg Na2CO3 [497-19-8] and 321 mg 3-(2'-iodoacetamido)-2,2,5,5-tetramethyl-1-pyrrolidinyl-1-oxyl [27048-01-7] to give 187 mg 3-(N-(1'-phenyl-2'-propyl)glycinamido)-2,2,5,5-tetramethylpyrrolidinyl-1-oxyl (II) [41370-71-2]. The Et2O ext. of a soln. of 3.68 g amphetamine sulfate [60-13-9] in 80 ml 0.5N NaOH was evapd., and the residue was dissolved in 50 ml benzene and treated with 3 ml diisopropylethylamine [7087-68-5] and 2.2 ml Et bromoacetate [105-36-2] to give the amino ester. The ester was dissolved in 50 ml 1:1 MeOH-1N NaOH, and the soln. was concd., and treated with HCl to pH 6 to give 900 mg N-carboxymethyl amphetamine [7738-39-8]. A suspension of the acid (700 mg) in 50 ml dry dioxane was treated with 20 ml of 12.5% phosgene in benzene, and the mixt. was evapd., redissolved in 20 ml/dry dioxane, and added over .5 hr to 2 g bovine serum albumin in 100 ml 2% NaHCO3 at 0.degree.. After 24 hr at 0.degree. and 18 hr at room temp., the reaction mixt. was dialyzed for 2 days against 35 l H2O at 0.degree., and lyophilized, giving 1.91 g conjugate contg. .apprx.76 I units per unit of albumin. For urine anal. for I, 25 .mu.l urine was mixed with 2.5 .mu.l 0.2M Na2Cr2O7 and added to a mixt. of 22 .mu.l I antibody (.gamma.-globulin), 144 .mu.l 2M pH8 borate buffer, and 99 .mu.l saline. Five .mu.l of a soln. of 105 .mu.l H2O and 160 .mu.l 2.8 .times. 10-5M I soln. was added, and the soln. was examd. by ESR spectroscopy. The method detected I concns. in the range of 0.7-1.5 .mu.g/ml. It also detected several other drugs with structures similar to I.

IC C07D451-12
NCL 260292000
CC 4-2 (Toxicology)
Section cross-reference(s): 1
IT **Albumins**, blood serum
RL: BIOL (Biological study)
(bovine, ligand analogs conjugation with)
IT 1-Piperidineacetic acid, 3-ethyl-2,6-dioxo-3-phenyl-, **albumin** conjugates
1-Piperidineacetic acid, 4-(ethoxycarbonyl)-4-phenyl-, **albumin** conjugates
1-Pyrrolidinyloxy, 3-[[9-(dimethylamino)-1,6-dioxo-7,7-

diphenyldecyl]amino]-2,2,5,5-tetramethyl-, **albumin** conjugates
2-Butenoic acid, 4-[hexahydro-5-(1-methylbutyl)-2,4,6-trioxo-5-pyrimidinyl]-, **albumin** conjugates
4-Piperidinecarboxylic acid, 1-methyl-4-phenyl-, bovine serum **albumin** conjugates
8-Azabicyclo[3.2.1]octane-2-carboxylic acid, 3-hydroxy-8-methyl-, **albumin** conjugates, [1R-(exo,exo)]-
8-Azabicyclo[3.2.1]octane-8-acetic acid, 3-(benzoyloxy)-2-(methoxycarbonyl)-, **albumin** conjugates, [1R-(exo,exo)]-
Acetic acid, [4-(2-aminopropyl)phenoxy]-, **albumin** conjugates
Acetic acid, [4-[2-(methylamino)propyl]phenoxy]-, **albumin** conjugates
Acetic acid, [4-[2-[(trifluoroacetyl)amino]propyl]phenoxy]-, anhydride with carbonochloridic acid, **albumin** conjugates
Acetic acid, [[(17.beta.)-17-hydroxyestra-1,3,5(10)-trien-3-yl]oxy]-, **albumin** conjugates
Acetic acid, [[[(17.beta.)-3,17-dihydroxyestra-1,3,5(10)-trien-6-ylidene]amino]oxy]-, **albumin** conjugates
Benzenebutanoic acid, .beta.-(methylamino)-, **albumin** conjugates
Benzenediazonium, 4-[(2-carboxy-3-hydroxy-8-azabicyclo[3.2.1]oct-8-yl)methyl]-, **albumin** conjugates, [1R-(exo,exo)]-
Benzenediazonium, 4-[[(2-carboxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl)oxy]carbonyl]-, hydroxide, inner salt, **albumin** conjugates, [1R-(exo,exo)]-
Benzenediazonium, 4-[[3-hydroxy-2-(methoxycarbonyl)-8-azabicyclo[3.2.1]oct-8-yl]methyl]-, **albumin** conjugates, [1R-(exo,exo)]-
Estrane, acetic acid deriv., **albumin** conjugates
Estrane, acetic acid deriv., **albumin** conjugates
L-Lysine, homopolymer, hydrobromide, carboxymethylmorphine conjugates
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT Glycine, N-(1-methyl-2-phenylethyl)-, **albumin** conjugates
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and **antibody** formation by)
IT 7738-39-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and **albumin** conjugation of)
IT 60-13-9
RL: RCT (Reactant)
(reaction of, with esters and **free radical** spin-labeling compds.)
IT 70-34-8 77-17-8 300-62-9
RL: RCT (Reactant)
(reaction of, with **free radical** spin-labeling compds.)
IT 57-27-2, reactions
RL: RCT (Reactant)
(with **free radical** spin-labeling compds.)

L25 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1968:10041 HCAPLUS
DOCUMENT NUMBER: 68:10041
TITLE: Reaction of serum albumin and glycyltryptophan free radicals with radioprotective substances
AUTHOR(S): Sapezhinskii, I. I.; Dontsova, E. G.
CORPORATE SOURCE: Inst. Khim. Fiz.,, Moscow, USSR
SOURCE: Biofizika (1967), 12(5), 794-8
CODEN: BIOFAI
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Effective consts. (1/mol. sec.) of interaction rates with free radicals of protein (Kb) and with glycyltryptophan are resp. listed for radioprotective substances: .beta.-mercaptoethylamine 4.6, 10.6; thiourea 2.9, 4.4; cysteine-HCl 2.6, 10.4; aminoethylisothiuronium-HBr 1.7, 3.3; aminopropylisothiuronium-HBr 1.6, 1.8; reduced glutathione 1.3, 3.5; propyl gallate 1.2, 0.4; Na diethyldithiocarbamate (I) 3.4 .times. 103, 103. The Kb with cysteine did not depend on protein concn. There is no correlation between the above-listed consts. and the reactivity of the compds. with protein. Mechanism of I reaction with protein-free radicals differed from the mechanism of the other compds. The protein under study was bull serum albumin.

CC 5 (Radiation Biochemistry)

IT **Albumins**, blood serum
RL: BIOL (Biological study)
(**radicals** (**free**) of, reaction with radiation-**damage** protective agents)

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=> dhis
DHIS IS NOT A RECOGNIZED COMMAND

=> d his

     (FILE 'WPIDS' ENTERED AT 09:31:09 ON 03 DEC 2001)
                DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 09:33:11 ON 03 DEC 2001
L1             88 S ^DAHK/SQSP
L2             19 S L1 AND SQL=4

     FILE 'HCAPLUS' ENTERED AT 09:34:32 ON 03 DEC 2001
L3             13 S L2
L4              4 S L3 AND RADICAL?
L5              4 S L1 AND RADICAL?
L6              4 S L4 OR L5
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=> fil wpids
FILE 'WPIDS' ENTERED AT 10:22:55 ON 03 DEC 2001
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FILE LAST UPDATED: 29 NOV 2001              <20011129/UP>
MOST RECENT DERWENT UPDATE            200170   <200170/DW>
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=> d his


     (FILE 'WPIDS' ENTERED AT 10:12:12 ON 03 DEC 2001)
                DEL HIS Y
L1           6073 S  ALBUMIN?
L2          13382 S FREE (3A) RADICAL#
L3             44 S L1 AND L2
L4              4 S L3 AND METAL?
L5          25638 S MARKER#
L6              2 S L3 AND L5
L7             97 S L1 (4A) (MODIF? OR ALTER? OR DAMAG?)
L8              2 S L2 AND L7
L9            531 S OXIDATIVE (4A) (DAMAG? OR STRESS?)
L10            14 S L9 AND L1
L11             1 S L10 AND L7
L12          1028 S ATOMIC (3A) SPECT?
L13             1 S L3 AND L12
L14             1 S L12 AND L9
L15             0 S DAHK
L16             9 S ASP ALA HIS LYS
L17             1 S ASPARTIC ACID (2W) ALANINE (2W) HISTIDINE (2W) LYSINE
L18            10 S L16 OR L17
L19             3 S L18 AND L1
L20             6 S L6 OR L11 OR L13 OR L14 OR L19
L21        783099 S  V OR AS OR CO OR SB OR CR OR MO OR MN OR BA OR ZN OR NI OR H
L22            11 S L3 AND L21
L23        654085 S VANADIUM OR ARSENIC OR COBALT OR ANTIMONY OR CHROMIUM OR MOLY
L24             5 S L23 AND L3
L25            14 S L22 OR L24
L26             5 S L20 NOT L25
L27            13 S L25 NOT L20

     FILE 'WPIDS' ENTERED AT 10:22:55 ON 03 DEC 2001

=> d .wp 120 1-6;d .wp 127 1-13

L20  ANSWER 1 OF 6  WPIDS COPYRIGHT 2001   DERWENT INFORMATION LTD
AN   2000-579163 [54]   WPIDS
DNN  N2000-428604       DNC C2000-172361
TI   New isolated peptide which mimics a carbohydrate epitope is useful for
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neuroprotection.
DC A96 B04 D16 S03
IN HERZBERG, U; NEUBERGER, T J; SCHACHNER, M; SIMON, M
PA (ACOR-N) ACORDA THERAPEUTICS
CYC 90
PI WO 2000050447 A1 20000831 (200054)* EN 212p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000028841 A 20000914 (200063)
ADT WO 2000050447 A1 WO 2000-US4730 20000224; AU 2000028841 A AU 2000-28841 20000224
FDT AU 2000028841 A Based on WO 200050447
PRAI US 2000-511956 20000223; US 1999-121327P 19990224; US 1999-256970 19990224; US 1999-155492P 19990923; US 1999-404431 19990923
AB WO 200050447 A UPAB: 20011129
NOVELTY - An isolated peptide (I) which mimics the carbohydrate epitope GlcA beta 1-->3Gal beta 1-->4GlcNAc or sulphate-3GlcA beta 1-->3Gal beta 1-->4GlcNAc is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated peptide comprising sequence (1) - (8) or one of the twelve 15 - 17 amino acid sequences provided in the specification;

(2) a method (M1) for promoting neural growth and/or remylenation and/or neuroprotection in vivo in the central nervous system (CNS) comprising administering (I), which is capable of overcoming inhibitory molecular cues found on glial cells and myelin and promoting neural growth;

(3) a method (M2) for enhancing memory comprising administering (I) to the brain of a mammal;

(4) a method (M3) for increasing synaptic efficacy in the CNS of a mammal comprising administering (I);

(5) a method (M4) for promoting neuroprotection and/or neuronal survival comprising administering (I);

(6) a method (M5) for inhibiting axonal cell death and enhancing myelenation and remylenation in the CNS comprising administering (I), which is capable of overcoming inhibitory molecular cues found on glial cells and myelin and promoting neural growth;

(7) a DNA sequence (II) which encodes (I);

(8) a unicellular host transformed with (II);

(9) a cloning and expression vector comprising (II);

(10) a method (M6) for detecting the presence or activity of (I) comprising:

(a) contacting a sample with a binding partner; and

(b) detecting whether binding has occurred, where detection of binding indicates the presence or activity of the peptide;

(11) a test kit for the demonstration of a molecule capable of binding GlcA beta 1-->3Gal beta 1-->4GlcNAc or sulphate-3GlcA beta 1-->Gal beta 1--> 4GlcNAc in a eukaryotic cellular sample comprising:

(a) a predetermined amount of a detectably (I);

(b) other reagents; and

(c) directions for use;

(12) a method (M7) for testing the ability of a drug or other entity to mimic (I) comprises:

(a) adding CNS neurons to a cell culture system;

(b) adding the drug or other entity to a cell culture system;

(c) measuring the neuronal outgrowth of the CNS neurons; and

(d) correlating a difference in the level of neuronal outgrowth of cells in the presence of the drug relative to a control culture to which no drug is added;

(13) a pharmaceutical composition comprising (I);

(14) a method (M8) for preventing, ameliorating or blocking viral infection comprising administering (I); and

(15) a method (M9) for preventing, ameliorating or blocking neuropathy comprising administering (I), where the neuropathy is viral mediated, immune mediated or the result of trauma.

X1a-X2a-X3a-X4a-X5a-Leu/Val-X6a-X7a-X8a-X9a-X10a-X11a-X12a-X13a-X14a (1);

Phe-Leu-His-Thr-Arg-Leu-X1b-X2b-X3b-X4b-X5b-X6b-X7b-X8b-X9b (2);

Phe-Leu-His-Thr-Arg-Leu-Phe-Val-X1c-X2c-X3c-X4c-X5c-X6c-X7c (3);

Phe-Leu-His-Thr-Arg-Leu-Phe-Val-Ser-Asp-Trp-Tyr-His-Thr (4);

Phe-Leu-His-Thr-Arg-Leu-Phe-Val (5);

Thr-Arg-Leu-Phe-Arg-(Val/Phe) (6);

Thr-Arg-Leu-Phe-(Arg)-Val (7); and

Thr-Arg-Leu-Phe (8).

Where:

X1a = Thr, Ser, Ala or Pro;

X2a = Leu, Ile, Val, Met, Phe, His, Trp or Asn;

X3a = Thr, Ser, Ala, His, Tyr, Phe, Trp, Asn, Asp or Glu;

X4a = Arg, Gln, Lys, Thr, Ser or Ala;

X5a = Val, Ile, Leu, Met, Arg, Gln or Lys;

X6a = Thr, Ser, Ala, Tyr, Phe, His, Trp, Asn, Leu, Ile, Val or Met;

X7a = Asp, Glu, Val, Leu, Ile, Met, Phe, Tyr, His, Trp or Asn;

X8a = Val, Ile, Leu, Met, Ser, Ala, Thr, Arg, Gln or Lys;

X9a = Tyr, Phe, His, Trp, Asp, Glu, Ile, Val, Leu, Met or Asn;

X10a = Arg, Gln, Lys, Trp, Tyr, Phe, His, Asn, Val, Ile, Leu, Met or Gly;

X11a = Gly, Tyr, Phe, His, Trp, Asn, Ser, Ala. Thr, Ile, Val, Leu or Met;

X12a = Arg, Gln, Lys, His, Asn, Tyr, Phe, Trp, Ile, Val, Leu or Met;

X13a = Leu, Val, Ile, Met, Thr, Ser or Ala;

X14a = Ser, Thr, Ala, Pro, Gyl, Arg, Gln or Lys;

X1b = Thr, Ser, Ala, Tyr, Phe, His, Trp, Asn, Leu, Ile, Val or Met;

X2b = Asp, Glu, Val, Leu, Ile, Met, Phe, Tyr, His, Trp or Asn;

X3b = Val, Ile, Leu, Met, Ser, Ala, Thr, Arg, Gln or Lys;

X4b = Tyr, Phe, His, Trp, Asp, Glu, Ile, Val, Leu, Met or Asn;

X5b = Arg, Gln, Lys, Trp, Tyr, Phe, His, Asn, Val, Ile, Leu, Met or Gly;

X6b = Gly, Tyr, Phe, His, Trp, Asn, Ser, Ala, Thr, Ile, Val, Leu or Met;

X7b = Arg, Gln, Lys, His, Asn, Tyr, Phe, Trp, Ile, Val, Leu or Met;

X8b = Leu, Val, Ile, Met, Thr, Ser or Ala;

X9b = Ser, Thr, Ala, Pro, Gly, Arg, Gln or Lys;

X1c = Val, Ile, Leu, Met, Ser, Ala, Thr, Arg, Gln or Lys;

X2c = Tyr, Phe, His, Trp, Asp, Glu, Ile, Val, Leu, Met or Asn;

X3c = Arg, Gln, Lys, Trp, Tyr, Phe, His, Asn, Val, Ile, Leu, Met or Gly;

X4c = Gly, Tyr, Phe, His, Trp, Asn, Ser, Ala, Thr, Ile, Val or Met;

X5c = Arg, Gln, Lys, His, Asn, Tyr, Phe, Trp, Ile, Val, Leu or Met;

X6c = Leu, Val, Ile, Met, Thr, Ser or Ala; and

X7c = Ser, Thr, Ala, Pro, Gly, Arg, Gln or Lys.

ACTIVITY - Nootropic; neuroprotective; antiparkinsonian.

No supporting biological data is given.

MECHANISM OF ACTION - None given.

USE - For enhancing memory for inhibiting the onset or progression, or treating the presence or consequences of Alzheimers disease or dementia. For inhibiting the development or onset or treating the

presence of apoptosis, necrosis, Parkinsons disease, multiple sclerosis and acute and chronic spinal cord injury (all claimed).
Dwg.0/20

L20 ANSWER 2 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-303843 [26] WPIDS
DNN N2000-226961 DNC C2000-092353
TI New method for the continuous detection of ischemic states comprises detecting and quantifying the existence of an alteration of the serum protein **albumin**.
DC B04 D16 S03
IN BAR-OR, D; LAU, E; WINKLER, J V
PA (ISCH-N) ISCHEMIA TECHNOLOGIES INC
CYC 90
PI WO 2000020840 A1 20000413 (200026)* EN 102p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 9964095 A 20000426 (200036)
EP 1125107 A1 20010822 (200149) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000020840 A1 WO 1999-US22905 19991001; AU 9964095 A AU 1999-64095 19991001; EP 1125107 A1 EP 1999-951710 19991001, WO 1999-US22905 19991001
FDT AU 9964095 A Based on WO 200020840; EP 1125107 A1 Based on WO 200020840
PRAI US 1999-115392P 19990111; US 1998-102738P 19981002; US 1998-165581 19981002; US 1998-165926 19981002
AB WO 200020840 A UPAB: 20000531

NOVELTY - A method (M1) for the continuous detection of ischemic states by detecting and quantifying the existence of an alteration of the serum protein **albumin**, is new.

DETAILED DESCRIPTION - A method (M1) for the continuous detection of ischemic states by detecting and quantifying the existence of an alteration of the serum protein **albumin**, is new.

M1 comprises:

(a) contacting a biological sample containing **albumin** from the patient with an excess quantity of a metal ion salt, where the metal ion binds to the N-terminus of naturally occurring human **albumin**, to form a mixture containing bound metal ions and unbound metal ions

(b) determining the amount of metal ions bound to the **albumin** N-terminus, and

(c) correlating the amount of bound metal ions to a known value to determine the occurrence or non-occurrence of an ischemic event.

INDEPENDENT CLAIMS are also included for the following:

(1) A method (M2) for detecting the occurrence or non-occurrence of an ischemic event in a patient comprising:

(a) detecting the amount of endogenous copper ions present in a purified **albumin** sample from the patient; and

(b) correlating the quantity of copper ions present with a known value to determine the occurrence or non-occurrence of an ischemic event;

(2) A method for ruling-out the existence of ischemia in a patient, where the patient possesses one or more cardiac risk factors, comprising:

(a) application of M1 or M2 to the patient;

(b) subjecting the patient to an exercise treadmill test followed by a second application of M1 or M2;

(c) comparing the results of the two applications of the method;

(3) A method for evaluation of a patient presenting with angina or angina-like symptoms to detect the occurrence or non-occurrence of a

myocardial infarction, comprising:

(a) application of M1 or M2 to the patient;

(b) application of an electrocardiographic test;

(c) correlating the results of step (a) with the results of the electrocardiographic test to determine the occurrence or non-occurrence of a myocardial infarction.

(4) A method for supplementing electrocardiographic results to determine the occurrence or non-occurrence of an ischemic event, is similar to the method of (3), except step (c) comprises correlating the results of step (a) with the results of the electrocardiographic test to determine the occurrence or non-occurrence of an ischemic event;

(5) A method for comparing levels of ischemia in patients at rest and during exercise, comprising application of the following steps at designated times:

(a) application of M1 or M2 at a first designated time;

(b) administration of an exercise treadmill test followed by a second application of the same method employed in step (a);

(c) comparing the results of step (a) with the results obtained in step (b); and

(d) repeating steps (a) and (b) at additional designated times, where results obtained designated at each designated time are compared;

(6) An immunoassay diagnostic kit for an ischemic event comprising:

(a) an excess quantity of a metal ion to mix with a patient sample which comprises naturally-occurring **albumin** and optionally **albumin** N-terminal derivatives, the naturally-occurring **albumin** forming a complex with the metal ion;

(b) a first elongated solid support having a first and a second end, the first end having a filter for application of the patient sample mixture, an area of immobilized antibody to the **albumin**-metal complex between the first end the second end, and an area of immobilized ligand to **albumin** proximate the second end, where after application of the mixture of patient sample and metal ion to the filter, the **albumin**-metal complex is immobilized at the area of immobilized antibody, and the **albumin** N-terminal derivatives migrate and bind to the **albumin** ligand proximate the second end;

(7) A metal affinity diagnostic kit for an ischemic event comprising a first elongated solid support having a first and a second end, the first end having a filter for application of a patient sample, an area of immobilized metal ion between the first and the second end, and an area of immobilized ligand to naturally occurring **albumin** or **albumin** N-terminal derivatives proximate the second end;

(8) A ligand directed to an epitope at the N-terminus of the **albumin** N-terminal derivative which lacks four, three, two or one N-terminal amino acids of a 585 amino acid sequence (I) defined in the specification;

(9) A ligand to an epitope at the N-terminus of a 585 amino acid sequence (II) defined in the specification;

(10) A calibrator composition comprising a predetermined molar ratio of naturally occurring albumin and a metal that complexes to the N-terminus of the albumin, where the complexed albumin and unbound albumin form when the composition is in aqueous solution, where the ratio is between 0.1:1 and 1:0.1;

(11) A method of calibrating an analyzer that detects or measures an ischemic event according to M1, comprising applying the solution of (10) to the analyzer to determine the amount of metal ions (preferably copper) bound to the albumin N-terminus, where the predetermined ration of albumin to metal serves as a standard for calibration;

(12) A method of detecting an albumin N-terminal derivative which lacks four, three, two, or one N-terminal amino acids of (I), comprising contacting a sample comprising the derivative with the ligand of (8);

(13) A method of detecting an albumin N-terminal derivative which is acetylated at its N-terminal Asp residue of (II), comprising contacting a sample comprising the derivative with the ligand of (9); and

(14) A calibrator composition comprising a predetermined molar ratio of naturally occurring albumin and albumin N-terminal derivatives, where the ratio is between 0. 1: 1 and 1:0.1.

USE - The methods are useful for detection of ischemic states. The methods are also useful for distinguishing perioperative ischemia from ischemia caused by , amongst other things, myocardial infarctions and progressive coronary artery disease.

ADVANTAGE - The method is rapid.

Dwg.0/19

L20 ANSWER 3 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-303746 [26] WPIDS
DNN N2000-226916 DNC C2000-092265
TI Sensitive **marker** for detection of **free radical** damage comprising modified **albumin**, useful for detecting diseases associated with **free radicals** such as neurodegenerative diseases and cancers.
DC B04 S03
IN BAR-OR, D; LAU, E
PA (DIAG-N) DIAGNOSTIC MARKERS INC
CYC 88
PI WO 2000020454 A1 20000413 (200026)* EN 36p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9962793 A 20000426 (200036)
EP 1117686 A1 20010725 (200143) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000020454 A1 WO 1999-US22746 19991001; AU 9962793 A AU 1999-62793 19991001; EP 1117686 A1 EP 1999-950055 19991001, WO 1999-US22746 19991001
FDT AU 9962793 A Based on WO 200020454; EP 1117686 A1 Based on WO 200020454
PRAI US 1998-165961 19981002; US 1998-102962P 19981002
AB WO 200020454 A UPAB: 20000531
NOVELTY - A **marker** (I) for the detection of **free radical** damage, comprising **albumin** which is modified in a manner resulting in inhibition of metal binding capacity of the N-terminus, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for detecting and quantifying (I) comprising:

(a) providing a biological sample containing **albumin**;

(b) providing a metal ion salt, where the metal ion is capable of binding to the N-terminus of unmodified **albumin**;

(c) contacting the biological sample with an excess quantity of the metal ion so that a mixture of bound and unbound ions is formed;

(d) determining the quantity of bound metal ions; and

(e) correlating the quantity of bound metal ions to a known value to determine the quantity of the **marker** present in the sample and to determine if the quantity is sufficient to indicate **free radical** damage;

(2) a method for detecting and quantifying (I) comprising:

(a) determining the quantity of copper ions present in a purified **albumin** sample; and

(b) correlating the quantity of the copper ions present in the sample with a known value to determine the quantity of the **marker** present in the sample and to determine if the quantity is sufficient to indicate **free radical** damage;

(3) a compound having the formula **Asp-Ala-His-Lys**-R, where R is any chemical group capable of providing a detectable signal when the compound is bound to a metal ion capable of binding to the N-terminus of unmodified human **albumin** ;

(4) an antibody (Ab1) binding to (I)

(5) an antibody (Ab2) that binds to the peptide **Asp-Ala-His-Lys**;

(6) an immunological assay conducted using (I) as an antigen;

(7) an immunological assay using Ab1 or Ab2;

(8) a method of monitoring or assessing a disease or condition comprising detecting and quantifying (I); and

(9) a kit for detecting or quantifying (I).

USE - The methods are useful for detecting diseases associated with **free radicals** including Parkinson's, Alzheimer's, cataractogenesis, atherosclerosis, diabetes mellitus, ischemia-reperfusion injury and certain toxicities. (I) is useful as a biochemical tag, allowing for sensitive detection and measurement of the efficacy of clinical drugs and therapeutics which result in the generation of **free radicals** or which act to limit **free radical** damage.

ADVANTAGE - (I) is a **marker** for the existence and detection and/or measurement of **free radical** damage which is highly sensitive and present in a majority of human fluids and tissues.

Dwg.0/0

L20 ANSWER 4 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1993-076649 [09] WPIDS
DNN N1993-058859 DNC C1993-033841
TI Method for detection of ischaemic states - by contacting serum or plasma sample with metal ions (e.g. cobalt) capable of binding to thiol gps..
DC B04 S03
IN BAR-OR, D; SOLOMONS, C
PA (DIAG-N) DIAGNOSTIC MARKERS INC; (ISCH-N) ISCHEMIA TECHNOLOGIES INC
CYC 23
PI WO 9303346 A1 19930218 (199309)*
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU BR CA JP KR NO
AU 9223187 A 19930302 (199326)
US 5227307 A 19930713 (199329) 6p
PT 100724 A 19930930 (199342)
US 5290519 A 19940301 (199409) 6p
NO 9400256 A 19940125 (199415)
EP 596925 A1 19940518 (199420) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 06509645 W 19941027 (199502)
BR 9206312 A 19950411 (199521)
EP 596925 A4 19960214 (199639)
AU 9710006 A 19970320 (199720)
AU 705300 B 19990520 (199931)
KR 239947 B1 20000115 (200116)
JP 3194952 B2 20010806 (200147) 9p
ADT WO 9303346 A1 WO 1992-US5668 19920710; AU 9223187 A AU 1992-23187 19920710; US 5227307 A US 1991-736583 19910726; PT 100724 A PT 1992-100724 19920724; US 5290519 A Div ex US 1991-736583 19910726, US 1993-16971 19930212; NO 9400256 A WO 1992-US5668 19920710, NO 1994-256 19940125; EP

596925 A1 EP 1992-915563 19920710, WO 1992-US5668 19920710; JP 06509645 W WO 1992-US5668 19920710, JP 1993-503561 19920710; BR 9206312 A BR 1992-6312 19920710, WO 1992-US5668 19920710; EP 596925 A4 EP 1992-915563 ; AU 9710006 A Div ex AU 1992-23187 19920710, AU 1997-10006 19970103; AU 705300 B Div ex AU 1992-23187 19920710, AU 1997-10006 19970103; KR 239947 B1 WO 1992-US5668 19920710, KR 1994-700225 19940125; JP 3194952 B2 WO 1992-US5668 19920710, JP 1993-503561 19920710

FDT AU 9223187 A Based on WO 9303346; US 5290519 A Div ex US 5227307; EP 596925 A1 Based on WO 9303346; JP 06509645 W Based on WO 9303346; BR 9206312 A Based on WO 9303346; AU 705300 B Previous Publ. AU 9710006; JP 3194952 B2 Previous Publ. JP 06509645, Based on WO 9303346

PRAI US 1991-736583 19910726; US 1993-16971 19930212

AB WO 9303346 A UPAB: 19990802

Detection of ischaemia in a patient comprises: (a) contacting a serum, plasma, fluid or tissue sample of the patient with metal ions, capable of binding to thiol gps. in the sample, to form a mixt. contg. sample bound metal ions and non-sample bound metal ions; and (b) detecting the amt. of non-sample bound metal ions to determine the amt. of thiol gps. in the sample.

Also claimed is a kit, for detecting the presence of an ischaemic event, comprising a metal salt and a colour-forming cpd. capable of forming a coloured cpd. with the metal salt.

USE/ADVANTAGE - In patients who have experienced an ischaemic event, the no. of thiol gps. in the proteins contained in the serum, plasma, fluid or tissue of the patient is reduced due to oxidn. by OH and peroxide radicals. The process quantifies protein-bound thiol gps. in a sample as a measure of **oxidative damage** to the sample due to the ischaemic event. The free metal ions remaining after complexation may be detected by conventional methods. The samples may be compared with samples from healthy patient

Dwg.0/0

L20 ANSWER 5 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1987-291654 [41] WPIDS

DNC C1987-123876

TI Measuring **oxidative damage** to cells - by chemiluminescence using complex of luminescer and serum **albumin**.

DC B04 D16

IN KIEI, J L

PA (MCLA-N) MCLAS TECHNOL INC

CYC 13

PI WO 8705941 A 19871008 (198741)* EN 65p
RW: AT BE CH DE FR GB IT LU NL SE
W: AU DK JP
AU 8773974 A 19871020 (198803)

ADT WO 8705941 A WO 1987-US686 19870324

PRAI US 1986-844001 19860325

AB WO 8705941 A UPAB: 19930922

**Oxidative damage** to living cells is measured by contacting the cells with a complex of a luminescer (I) and serum **albumin** (II), where (I) is non-covalently bonded to (II), and triggering a light-generating reaction.

(I) is luminol and (II) is bovine serum **albumin** (BSA). The complex may also contain a heme protein (III) in the form of a conjugate formed from (I), (II), (III) and a polyamino cpd. (esp. lysine). The conjugate may be crosslinked with a bifunctional cpd., e.g. glutaraldehyde. After contacting the cells with the complex, they are treated with a reducing agent (esp. KBH4) and luminescence is triggered by adding a base. When the complex contains (III), luminescence may also be triggered by heating.

USE/ADVANTAGE - The process may be used as a diagnostic tool for detecting exposure to exogenous oxidants, ionising radiation or hyperthermia or for detecting deficiencies in free-radical-scavenging enzymes. Use of (II) eliminates the need for an oxidase-peroxidase system. The (I)-(II) complex is bound by cell-surface aldehyde gps. (formed by peroxidative damage), and the bound complex produces so much more luminescence than the unbound complex that a homogeneous assay may be performed without a washing step.
0/14

L20 ANSWER 6 OF 6 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1966-30621F [00] WPIDS
TI Organic molecules providing **free radicals** for tagging of biomolecules by electron-spin resonance - A. of formula - where C1 and C2 are tert. C atoms.
DC B04 E13 J04
PA (SYNT) SYNVAR ASSOC
CYC 6
PI FR 1501115 A (196800)*
GB 1169872 A (196801)
US 3453288 A (196801)
US 3481952 A (196801)
US 3489522 A (197002)
CA 839265 A (197016)
JP 45010138 B (197016)
JP 46019520 B (197121)
DE 1620411 A 19700430 (198422)
PRAI US 1965-512793 19651209
AB FR 1501115 A UPAB: 19930831
Organic molecules providing **free radicals** for tagging of
biomolecules by electron-spin resonance:-
A. of formula:-
where C1 and C2 are tert. C atoms bound directly to c or fluorine atoms; A is at least one organic group having a total of 6 valencies available for bonding to atoms C1 and C2 and contains a functional group (not 2,4-dinitrophenyl) capable of forming a linkage with a biol. active molecule.
B. Esp. of formula
where R', R2, R3, R4 = lower alkyl, B = alkylene which completes the heterocyclic ring; X = organic group contng. a functional group (not 2,4-dinitrophenyl) capable of forming a linkage with a biol. active molecule, esp. isocyanate, isothiocyanate or a maleimide nucleus.
Tagging of various parts of molecules with specific **markers** allows one to follow the course of biol. reactions and to elucidate chemical structure. The **markers** are stable in aqs. media. For example the action of pepsin on bovine serum **albumin** may be followed by tagging the **albumin** with 2,2,5,5-tetramethyl-3-isocyanatopyrrolidine-1-oxide. Fluorescent **markers** may be incorporated in the molecule of the electron-spin resonance **marker**.

L27 ANSWER 1 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-483075 [52] WPIDS
DNC C2001-144788
TI Gel-based medium composition useful for storage and transport of cell

samples, comprises a cell maintenance and preservation medium and a gelling agent.

DC B04 D16 D22
IN BAUST, J G; BAUST, J M; VAN BUSKIRK, R
PA (BIOL-N) BIOLIFE SOLUTIONS INC
CYC 21
PI WO 2001050851 A2 20010719 (200152)* EN 22p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: CA JP
ADT WO 2001050851 A2 WO 2001-US912 20010112
PRAI US 2001-176009 20010111; US 2000-176009P 20000114
AB WO 200150851 A UPAB: 20010914
NOVELTY - A gel-based medium composition contains at least one cell maintenance and preservation medium and at least one gelling agent, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for storing cell samples in a gel-based medium composition, comprising:

(a) warming the composition to melt the gelling agent;

(b) suspending cell samples in a cell preservation solution without a gelling agent;

(c) mixing the suspended cell samples with the warmed gel-based medium composition;

(d) cooling the cell samples to solidify the gelling agent; and

(e) transferring the cooled cell samples to a desired storage temperature, preferably -196 - 37 deg. C.

The cooled cell samples are transported in a gelled state.

USE - For storage and transport of cell samples in the form of organs, tissues, cell monolayer and single cells, which are obtained from plants, animals, fungi, microbes or humans at normothermic, hypothermic and cryopreservative temperature, preferably -196 - 37 deg. C (claimed).

ADVANTAGE - The composition protects the cell samples from the mechanical, physiological and biochemical stresses inherently associated with liquid preservation techniques. The gelled preservation media enables preservation of tissue in a semi-solid preservation matrix keeping the tissue structurally intact while affording the same protective benefits to the tissue as is conferred to individual cells and cell monolayers. The reduction in the external mechanical shipping forces experienced by the tissues shipped in the gel medium markedly improves tissue viability following preservation.

Dwg.0/8

L27 ANSWER 2 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-407935 [43] WPIDS
DNC C2001-123484
TI Dialysis solution including a polyglycol osmotic agent, providing reduced dialysis time, and/or **free radical** scavenger reducing complications due to production of degradation products from gamma sterilization.
DC A96 B05
IN SIMON, J; STRICKLAND, A D; STROM, R M
PA (DOWC) DOW CHEM CO
CYC 90
PI WO 2001028544 A2 20010426 (200143)* EN 10p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ YU ZA ZW
AU 2000078795 A 20010430 (200148)

ADT WO 2001028544 A2 WO 2000-US28523 20001013; AU 2000078795 A AU 2000-78795 20001013
FDT AU 2000078795 A Based on WO 200128544
PRAI US 1999-159810P 19991015
AB WO 200128544 A UPAB: 20011129
NOVELTY - A dialysis solution including a polyglycol osmotic agent having a molecular weight 500-20,000 daltons, provides an improved osmotic gradient resulting in reduced dialysis times and/or reduced volumes of required dialysis solution. Also **free radical** scavengers are used to reduce complications due to degradation products from gamma sterilization.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(a) use of the solutions for performing dialysis;
(b) use of a filter to reduce introduction of bacteria into the peritoneal cavity; and
(c) a dialysis solution comprising a **free radical** scavenger.
USE - For use in hemodialysis or peritoneal dialysis.
ADVANTAGE - Use of a **free radical** scavenger in the dialysis solution allows sterilization of the solution using gamma radiation with minimal damage to solution components while maintaining a physiological pH.
Dwg.0/0

L27 ANSWER 3 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-572048 [53] WPIDS
DNC C2000-170525
TI Negatively charged microporous membrane, useful e.g. for recovering charged biomolecules from a gel, comprises porous substrate and crosslinked coating with pendant anionic groups.
DC A11 A14 A89 B04 D16 G02 J01 J04
IN HOU, C; KONSTANTIN, P; YANG, Y
PA (PALL) PALL CORP
CYC 90
PI WO 2000050160 A1 20000831 (200053)* EN 33p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000033764 A 20000914 (200063)
ADT WO 2000050160 A1 WO 2000-US4745 20000225; AU 2000033764 A AU 2000-33764 20000225
FDT AU 2000033764 A Based on WO 200050160
PRAI US 1999-121668P 19990225
AB WO 200050160 A UPAB: 20001023
NOVELTY - Negatively charged microporous membrane (A) comprises a porous substrate (B) and a crosslinked coating (C) having pendant anionic groups.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) (A) having dynamic protein-binding capacity of at least 25 mg lysozyme/ml, and in which (C) provides a fixed negative charge;
(2) a device containing (A);
(3) a method for preparing (A);
(4) a method for separating positively charged molecules (D) from a fluid by retaining them on (A); and
(5) a process for transferring biomolecules (E) from an electrophoretic gel by treating the gel with (A).

USE - (A) are especially used, as ion-exchange materials, for removal (purification) of positively charged biomolecules (especially proteins, polypeptides, amino acids and nucleic acids) from solution, specifically for transferring them from an electrophoretic gel. Other applications are purification of human **albumin** from serum; in therapeutic fractionation of blood; separation of components from genetically engineered cell cultures or fermentation broths, and purification of viral vaccines and viral gene therapy vectors.

ADVANTAGE - (A) have high charge density; water-flow rates (e.g. 25-100 ml/min/square cm under 24 inches of **mercury**) and dynamic binding capacity (25-120 mg lysozyme/ml) but low non-specific protein binding. Proteins do not leach, before breakthrough; the membranes are practically free from grafts or covalent links to the substrate, and they can be prepared relatively simply. Where (A) includes a hydrophilic monomer, the distance between anionic groups is increased, reducing inter- and intra-chain associations, making the negative charges more readily available for interaction with positively charged substances.

DESCRIPTION OF DRAWING(S) - The figure depicts the breakthrough curve for lysozyme obtained from a membrane as described in the patent.
Dwg.0/3

L27 ANSWER 4 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-442393 [38] WPIDS
DNN N2000-330083 DNC C2000-134555
TI Reagents for assaying conjugated bilirubin contain chelating agent, metal ion and/or metal complex to inhibit reactivity with unconjugated bilirubin and **albumin**-bonded bilirubin.
DC B04 D16 J04 S03
IN MORIMOTO, Y
PA (NNTR) NIPPON SHOJI KK; (AZWE-N) AZWELL INC
CYC 20
PI WO 2000036140 A1 20000622 (200038)* JA 28p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: US
JP 2000166595 A 20000620 (200040) 10p
ADT WO 2000036140 A1 WO 1999-JP6820 19991206; JP 2000166595 A JP 1998-352611 19981211
PRAI JP 1998-352611 19981211
AB WO 200036140 A UPAB: 20000811
NOVELTY - Reagents for assaying conjugated bilirubin comprise agents for assaying bilrubin, and a chelating agent, metal ion and/or metal complex as reagents which selectively inhibit reactivity with unconjugated bilrubin and/or **albumin**-bonded bilirubin, are new.

USE - The reagents are useful for assaying conjugated bilirubin especially in the presence of unconjugated bilrubin and/or **albumin** -bonded bilirubin e.g. for detecting or monitoring hepatic disorders, diseases and function.

ADVANTAGE - The assay is selective for bilirubin as the reagents inhibit the reactivity of unconjugated bilirubin and/or **albumin** -bonded bilirubin.
Dwg.0/0

L27 ANSWER 5 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-293112 [25] WPIDS
DNC C2000-088635
TI Mutant human beta-globin polypeptides used for generating a blood substitute to supplement the oxygen-carrying capacity of a patient's blood comprises substitution or deletion of native cysteine residues.
DC B04 D16
IN FRONTICELLI, C

PA (UTEM) UNIV TEMPLE
CYC 90
PI WO 2000018802 A1 20000406 (200025)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9965041 A 20000417 (200035)
EP 1117690 A1 20010725 (200143) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000018802 A1 WO 1999-US22756 19990930; AU 9965041 A AU 1999-65041 19990930; EP 1117690 A1 EP 1999-953002 19990930, WO 1999-US22756 19990930
FDT AU 9965041 A Based on WO 200018802; EP 1117690 A1 Based on WO 200018802
PRAI US 1998-102640P 19981001
AB WO 200018802 A UPAB: 20000524

NOVELTY - A human beta -globin mutant polypeptide (I) comprising the amino acid sequence of normal human beta -globin modified by the substitution or deletion of Cys residues at positions 93 and 112 and the substitution of a Cys for a non-Cys residue at one other position in the polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid sequence (II) encoding a mutant beta -globin polypeptide (III) which has a defined sequence of 146 amino acids given in the specification;

(2) a vector comprising a promoter operably linked to (II) capable of directing the expression of a mutant beta -globin polypeptide;

(3) a host cell transformed with the vector of (2);

(4) a method for producing a human beta -globin mutant polypeptide comprising growing a culture of transformed host cells of (3) under conditions conducive to the expression of the polypeptide by the host cells;

(5) a modified human hemoglobin (IV) comprising (I) or (III);

(6) a polymeric hemoglobin (V) comprising (IV) where adjacent hemoglobins are covalently bonded to each other by one or more disulfide bridges formed by cysteine amino acid residues;

(7) a blood substitute comprising (V);

(8) a method of supplementing the oxygen-carrying capacity of a patient's blood comprising administering the blood substitute of (7); and

(9) a mutant human alpha -globin polypeptide (VI) comprising the amino acid sequence of normal human alpha -globin modified by the substitution or deletion of Cys at position 104.

ACTIVITY - Antianemic.

No biological data.

MECHANISM OF ACTION - Oxygen-carrier.

USE - The mutant alpha and beta -globin polypeptide sequences can be used to generate a modified human hemoglobin which is used to prepare a blood substitute for supplementing the oxygen-carrying capacity of a patient's blood (claimed). The blood substitute may be administered to any patient in a situation requiring supplementation of the oxygen-carrying capacity of the patient's blood.

ADVANTAGE - The mutant hemoglobin provided has high oxygen carrying capacity but low oncotic pressure which makes it useful as a blood substitute. A stable preparation of homogenous polymers is provided with the same characteristics unlike heterogeneous polymers of the prior art whose properties are difficult to control.

Dwg.0/3

L27 ANSWER 6 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-194945 [17] WPIDS
DNC C2000-060366
TI Polymer carriers for keratinocyte cultivation to cover skin defects e.g. burns, trophic ulcers and bedsores, avoid presence of feeder cells from cultivation system loading immunological system.
DC A12 A14 A96 B04 D16
IN DVORANKOVA, B; LABSKY, J; SMETANA, K; VACIK, J
PA (UYKA-N) UNIV KARLOVA; (UYKA-N) UNIV KARLOVY 1 LEKARSKA FAKULTA; (UYKA-N) UNIV KARLOVY 3 LEKARSKA FAKULTA; (MAKR-N) USTAV MAKROMOLEKULARNI CHEM AVCR
CYC 82
PI WO 9964563 A1 19991216 (200017)* EN 30p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9940293 A 19991230 (200022)
CZ 9901946 A3 20010117 (200107)
CZ 9901947 A3 20010117 (200107)
ADT WO 9964563 A1 WO 1999-CZ17 19990609; AU 9940293 A AU 1999-40293 19990609; CZ 9901946 A3 CZ 1999-1946 19990602; CZ 9901947 A3 CZ 1999-1947 19990602
FDT AU 9940293 A Based on WO 9964563
PRAI CZ 1999-1947 19990602; CZ 1998-1803 19980610; CZ 1999-1946 19990602
AB WO 9964563 A UPAB: 20000405
NOVELTY - Polymer carriers for keratinocyte cultivation prepared by radical polymerization of polymerization mixture containing (weight%): polymerizable monomers (1-95), crosslinker (0-10), initiator (0-10), solvent (0-60), polymerizable saccharide or disaccharide derivatives (0-60), polymerizable sterically hindered amine derivatives (0-50), polymerizable alpha -amino acid derivatives (0-30) or their reactive derivatives.

ACTIVITY - Wound healing; burn healing; ulcer healing; bed sore healing.

USE - Used for cultivation of keratinocytes (claimed) to cover large skin defects such as burns, trophic ulcers and bedsores. Three standard polymer carriers and ten test polymer carriers were tested for adhesion of human keratinocytes after preincubation with bovine serum in presence of mouse fibroblasts or after adsorption of bioactive saccharides in absence of mouse fibroblasts. Adhesion of four test compounds was batter compared with the three standards, although activation of the base using sugars was necessary. Four test carriers showed very good keratinocyte cultivation, with keratinocytes adhering and growing without prior pre-incubation with bioactive polysaccharides.

ADVANTAGE - Avoids presence of feeder cells from cultivation system loading patient's immunological system. Does not possess properties that suppress formation of **free radicals** or reactive oxygen products to healing of affected tissues difficult. Allows application of autologous and allogenic cells to stimulate healing. Immunological loading of patient is lower and process of keratinocyte transplantation is simpler and more effective.
Dwg.0/0

L27 ANSWER 7 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-580278 [49] WPIDS
DNC C1999-168770
TI Crosslinkable macromer systems for use in the preparation of matrices.

DC A11 A12 A14 A18 A35 A60 A96 B07 D22 E19
IN ANDERSON, A B; CHUDZIK, S J
PA (SURM-N) SURMODICS INC
CYC 23
PI WO 9947129 A1 19990923 (199949)* EN 41p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP MX
US 6007833 A 19991228 (200007)
AU 9929035 A 19991011 (200008)
US 6156345 A 20001205 (200066)
EP 1063975 A1 20010103 (200102) EN
R: DE ES FR GB IE IT
ADT WO 9947129 A1 WO 1999-US5244 19990311; US 6007833 A Provisional US 1998-78607P 19980319, US 1998-121248 19980723; AU 9929035 A AU 1999-29035 19990311; US 6156345 A Provisional US 1998-78607P 19980319, Div ex US 1998-121248 19980723, US 1999-469976 19991221; EP 1063975 A1 EP 1999-909954 19990311, WO 1999-US5244 19990311
FDT AU 9929035 A Based on WO 9947129; US 6156345 A Div ex US 6007833; EP 1063975 A1 Based on WO 9947129
PRAI US 1998-121248 19980723; US 1998-78607P 19980319; US 1999-469976 19991221
AB WO 9947129 A UPAB: 19991124
NOVELTY - Crosslinkable macromer system comprising one or more polymers providing pendent polymerizable and pendent initiator groups and where the system is adapted for polymerization to form a matrix for in vivo application, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method of forming a polymeric matrix adapted for in vivo application, comprising applying the aforementioned macromer system to a substrate and cross-linking the system by **free radical** polymerization;

(2) a polymeric matrix adapted for in vivo application, consisting of the aforementioned macromer system which has been crosslinked by **free radical** polymerization.

USE - The matrix is used for cell immobilization, in the preparation of tissue adhesives and sealants, in controlled drug delivery, as well as in situ device formation (e.g. in the preparation of three-dimensional bodies for implants). Polymeric matrices can also be used in wound dressing, tissue replacement/scaffolding, cellular encapsulation.

ADVANTAGE - The macromer system has advantages over the use of polymerizable macromers and separate, low molecular weight initiators e.g. optimal combination of non-toxicity, efficiency and solubility. A collagen scaffolding containing a bone morphogenic protein was prepared from a solution of liquid macromer consisting of polymerizable collagen (5 w/v%) plus photoderivatized polyacrylamide in phosphate buffered saline (pH 7.4) which was treated with bone morphogenic protein (BMP-7) (50 mu g/ml, 0.005 w/v%). Aliquots (150 mu l) of the above solution were placed in molds (8 mm diameter, 3 mm high) and were illuminated for 10 seconds with a Dymax lamp to solidify the collagen scaffolding. Control disks of solidified scaffolding were prepared via the same protocol, except that BMP-7 was not added. The scaffolding was evaluated for stimulation of bone growth in a rat cranial onlay implant model. When evaluated histologically, the scaffolding containing BMP-7 showed extensive bone formation in the space originally occupied by the collagen disk. The amount of bone that formed with the controls was less than 25% of that observed with the BMP-7-containing disks, thus demonstrating that the solidified collagen scaffolding greatly enhanced BMP-stimulated bone formation.
Dwg.0/0

L27 ANSWER 8 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-243660 [20] WPIDS
DNC C1999-071030
TI Preventing or treating cell, tissue, organ or animal for reperfusion injury.
DC B03 B05 D16 D22
IN DODD-O, J M; PEARSE, D B
PA (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE
CYC 82
PI WO 9912539 A1 19990318 (199920)* EN 36p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9892261 A 19990329 (199932)
US 6090851 A 20000718 (200037)
ADT WO 9912539 A1 WO 1998-US18735 19980909; AU 9892261 A AU 1998-92261 19980909; US 6090851 A Provisional US 1997-58446P 19970910, Provisional US 1998-71188P 19980112, US 1998-150069 19980909
FDT AU 9892261 A Based on WO 9912539
PRAI US 1998-71188P 19980112; US 1997-58446P 19970910; US 1998-150069 19980909
AB WO 9912539 A UPAB: 19990525
NOVELTY - Preventing or treating a cell, tissue, organ or animal for reperfusion injury comprises administration of a reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase inhibitor to the cells, tissues, organs or animals.

MECHANISM OF ACTION - NADPH-oxidase inhibitor.

17 Sheep lungs were subjected to 30 minutes of ischaemia and 180 minutes of reperfusion with autologous blood. Diluent or 3 mM, 0.3 mM or 0.03 mM apocynin was administered to the pulmonary artery early in ischemia and the reservoir before perfusion. After reperfusion, the lungs were excised and subjected to increased static vascular pressures to measure the reflection coefficient for **albumin**, the filtration coefficient and extravascular lung water.

Results showed that 3 mM apocynin completely prevented decrease in reflection coefficient of **albumin** and the increase in extravascular lung water caused by ischemia, which showed that NADPH oxidase contributed to reperfusion injury in sheep lungs.

USE - Used to treat or prevent reperfusion injury associated with surgical procedures, especially cardiac surgery involving cardiopulmonary bypass, or transplantation of cells, tissue or an organ including lungs, heart, liver, intestine, pancreas, kidney, brain or limb (claimed). The method may be used to treat reperfusion injuries to a cell, whether in vitro for transplantation or research or in vivo including reperfusion injuries due to ischemia or hypoxia. The reperfusion injury treated may be due to direct exposure of a cell, tissue, organ or organism to reperfusion injury-inducing symptoms e.g. ischemia or hypoxia and/or indirect exposure such as exposure to another cell, tissue or organ exposed to reperfusion injury-inducing conditions e.g. ischemia or hypoxia. The injury may be associated with reperfusion-stimulated neutrophil activation such as that associated with a surgical procedure, e.g. cardiopulmonary bypass that involves pulmonary, cardiac and vascular dysfunction, cell/tissue/organ transplantation, such as orthotopic lung transplant, pulmonary embolus, thoracic surgery involving prolonged compression of the lung, stroke, trauma, seizure, myocardial infarction, angioplasty, ischemic bowel syndrome, ulcers, skin and muscle flaps (e.g. generated during injury or surgery), hypothermia (e.g. frostbite), reattachment of a body part and

neutrophil activation-associated damage of the lung, liver and kidney associated with distal ischemia reperfusion injury.

ADVANTAGE - In contrast to prior-art neutrophil-depleting agents, (I) are safe when given systemically for weeks or months. In contrast to prior-art **free-radical** scavenging agents, (I) do not result in production of potentially dangerous compounds such as hydrogen peroxide. In contrast to prior-art agents that increase intracellular cyclic AMP, (I) completely block reperfusion injury to the lung without activating ubiquitous signal transduction system that may **lead** to side-effects.

Dwg.0/0

L27 ANSWER 9 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-335297 [30] WPIDS
DNC C1998-103984
TI New organo-selenium and seleno-sulphide antioxidant agents - inhibit TNF induced interleukin release, use to preserve organs for transplants, inflammation, e.g., bowel, ARDS, glaucoma and AIDS.
DC B05
IN CHAUDIERE, J; ERDELMEIER, I; MOUTET, M; TAILHAN-LOMONT, C; YADAN, J; CHAUDIERE, J R; TAILHAN, L C; YADAN, J C
PA (OXIS-N) OXIS ISLE OF MAN LTD; (OXIS-N) OXIS INT SA
CYC 28
PI EP 850924 A1 19980701 (199830)* EN 48p
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
FR 2757857 A1 19980703 (199833)
AU 9852740 A 19980702 (199837)
CA 2225903 A 19980627 (199841)
JP 10330355 A 19981215 (199909) 26p
US 5973009 A 19991026 (199952)
US 6040328 A 20000321 (200021)
EP 850924 B1 20010314 (200116) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69704255 E 20010419 (200129)
AU 736842 B 20010802 (200152)
ES 2157524 T3 20010816 (200156)
ADT EP 850924 A1 EP 1997-204070 19971223; FR 2757857 A1 FR 1996-16103 19961227; AU 9852740 A AU 1998-52740 19980127; CA 2225903 A CA 1997-2225903 19971224; JP 10330355 A JP 1998-561 19980105; US 5973009 A US 1997-997669 19971223; US 6040328 A Div ex US 1997-997669 19971223, US 1999-387593 19990831; EP 850924 B1 EP 1997-204070 19971223; DE 69704255 E DE 1997-604255 19971223, EP 1997-204070 19971223; AU 736842 B AU 1998-52740 19980127; ES 2157524 T3 EP 1997-204070 19971223
FDT US 6040328 A Div ex US 5973009; DE 69704255 E Based on EP 850924; AU 736842 B Previous Publ. AU 9852740; ES 2157524 T3 Based on EP 850924
PRAI FR 1996-16103 19961227
AB EP 850924 A UPAB: 19980730
Organoselenium compounds of formula (I), and their salts are new: R = H or CR1R2-A-B; R1, R2 = lower alkyl, aryl (optionally substituted) or lower aralkyl (optionally substituted); A = **CO** or (CR3R4)n; B = NR5R6, N+R5R6R7 -, OR5 or SR5; Ar = optionally substituted phenyl group or heterocyclyl, provided R = C(R1R2)-A-B; or Ar = a different heterocyclyl, provided R = H; Z = O, S or NR5; X = Ar(R)-Se, -S-glutathione, -S-N-acetylcysteine, -S-cysteine, -S-penicillamine, -S-**albumin**, -S-glucose or one of eight amide containing groups; R3, R4 = H, lower alkyl, aryl (optionally substituted) or lower aralkyl (optionally substituted); R5 = R3, heteroaryl (optionally substituted), lower heteroaralkyl (optionally substituted), lower alkylcarbonyl, arylcarbonyl, lower alkylsulphonyl or arylsulphonyl; R6, R7 = R3, heteroaryl (optionally

substituted) or lower heteroaralkyl (optionally substituted); n = 0-1; X+ = cation; and Y- = anion; provided that when: (a) R = CR1R2CR3R4-B (where B = NR5R6 or N+NR5R6R7 Y-); and X = Ar(R)-Se- (where Ar = phenyl (optionally substituted)) then CR1R2 is different from CR3R4; and (b) Ar = phenyl; R = CR1R2-CO-B (where B = NH2, NHCH3, NHCH2Ph or NHPh; and X = Ar(R)-Se- then R1 and R2 are not both CH3.

USE - (I) are useful as antioxidants, particularly for preserving media of grafts for transplantation of organs, e.g. hearts, livers, kidneys and lungs. (I) are used in antioxidant compositions useful for the treatment of: (a) physiopathological conditions in which an over production of cytotoxic hydroperoxides contribute to impairments of cells or tissues; (b) inflammatory and/or ischaemic cardio- and cerebrovascular pathologies, e.g. arterial restenoses following angioplasty, arterial stenoses following artery allografts, treating intermittent claudation of obstructive ischaemia and treatments of cerebrovascular accidents of ischaemic origin; (c) inflammatory and/or ischaemic digestive pathologies, e.g. acute inflammation of the bowel (Crohn's disease and haemorrhagic rectocolitis); (d) inflammatory and/or ischaemic respiratory pathologies e.g. adult respiratory distress syndrome (ARDS) and infant respiratory distress syndrome (IRDS); (e) glaucoma; (f) cataracts; (g) acute ophthalmic allergies; (i) impairments of the retina associated with macular degeneration; (j) viral infections causing immuno-deficiency e.g. acquired immuno deficiency distress syndrome (AIDS); and (k) post-radiotherapy fibroses (all claimed). The composition is used for the treatment of any physiopathological condition in which an over-production of cytotoxic hydroperoxides contributes to the functional impairments of cells or tissues. This over-production of hydroperoxide can be due: (i) to the activation of the intra-cellular metabolic pathways such as those of the flavine or cytochrome P-450 oxygenases, lipoxygenases and monoamine oxidases; (ii) to the activation of enzymes contained in endothelial cells (xanthine oxidase, 15-lipoxygenase) or in blood platelets (cyclooxygenase and 12-lipoxygenase); (iii) to the activation, by cytokines such as TNF-A, of inflammatory and/or immune cells such as neutrophils, macrophages or lymphocytes; (iv) to an intoxication by a **free-radical** generating xenobiotic; or (**v**) to a voluntary irradiation, such as practised during a radiotherapy, or an accidental irradiation (all claimed).

ADVANTAGE - Preparations of these compounds by the present route are easy to carry out and give good yields. In particular, very few 4(5)-selenoimidazoles have been prepared in the literature, either by use of silyl protections, or from 4-halo-imidazoles and selenourea or NaSeH. Dwg.0/3

L27 ANSWER 10 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-007206 [01] WPIDS
DNC C1994-002820
TI Modified arabino galactan as carrier for therapeutic agents e.g. antivirals or anti sense DNA - provides targetted delivery to cells with the asialo glyco protein receptor, esp. hepatocyte(s).
DC A96 B04 B07 D16
IN ENRIQUEZ, P; JOSEPHSON, L; JUNG, C; PALMACCI, S; ENRIQUES, P
PA (ADMA-N) ADVANCED MAGNETICS INC
CYC 18
PI WO 9325239 A1 19931223 (199401)* EN 35p
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: CA JP NO
NO 9404838 A 19950217 (199516)
EP 646018 A1 19950405 (199518) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 07507794 W 19950831 (199543) 10p

ADT WO 9325239 A1 WO 1992-US5091 19920617; NO 9404838 A WO 1992-US5091 19920617, NO 1994-4838 19941214; EP 646018 A1 EP 1992-914217 19920617, WO 1992-US5091 19920617; JP 07507794 W WO 1992-US5091 19920617, JP 1994-501422 19920617
FDT EP 646018 A1 Based on WO 9325239; JP 07507794 W Based on WO 9325239
PRAI EP 1992-914217 19920617; WO 1992-US5091 19920617; NO 1994-4838 19941214
AB WO 9325239 A UPAB: 19940217
Carrier which forms a complex with a therapeutic agent (I) for delivery to a cell receptor on the surface of target tissue comprises arabinogalactan (**AG**) modified by a functional residue to produce a deriv. which retains affinity for the receptor.

Pref. **AG** is modified at one or more OH sites; the functional gp. introduced is phosphoryl, SH, NH2, halo, acylimidazole or COOH, or the functional residue is a polymer, pref. dextran, dextrin, **albumin** or poly-L-lysine.

Pref. antiviral agents are acyclovir; adenine arabinoside-5'-monophosphate (Ara-AMP), or Ara-A; the protective agent is S-2-(3-aminopropylamino)-ethylthiophosphoric acid; scavengers are e.g. melanin, cysteamine derivs. or Vitamin E derivs.

USE/ADVANTAGE - The complexes are used to deliver, as (I), antivirals; radio- or chemo-protective agents, **free radical** scavengers; polypeptides, antibodies or their fragments (directed e.g. against hepatitis B virus); DNA (partic. antisense) or antiinflammatory steroids. They are targetted to cells carrying the asialoglycoprotein receptor, esp. hepatocytes, and precise targetting should reduce side effects of (I).

Unlike glycoproteins previously suggested as carriers, **AG** is unlikely to be contaminated by human viruses; can tolerate contact with organic solvent; has only a limited variety of reactive sites; has low toxicity and antigenicity, and has natural affinity for the specified receptor (eliminating need for a deasialylation reaction).
Dwg. 0/0

L27 ANSWER 11 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-235761 [33] WPIDS
DNC C1989-104985
TI New covalent conjugate of 3-bonded vinca alkaloid - with protein carrier useful as anticancer agents with controlled targetting and reduced toxicity.
DC B02
IN BHUSHANA, R; COLLARD, M P; DEJONGHE, J P; TROUET, A; COLLARD, M; DEJONGHE, J
PA (IREC-N) IRE CELLTARG SA; (WALL-N) LA REGION WALLONNE; (IREC-N) IRE-CELLTARG SA
CYC 16
PI EP 328446 A 19890816 (198933)* FR 16p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
FR 2626882 A 19890811 (198939)
JP 02152992 A 19900612 (199029)
US 5024835 A 19910618 (199127) 11p
EP 328446 B1 19940720 (199428) FR 28p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 68916820 E 19940825 (199433)
ES 2057157 T3 19941016 (199442)
CA 1336119 C 19950627 (199533) FR
JP 2930965 B2 19990809 (199937) 13p
ADT EP 328446 A EP 1989-400334 19890207; US 5024835 A US 1989-306639 19890203; EP 328446 B1 EP 1989-400334 19890207; DE 68916820 E DE 1989-616820 19890207, EP 1989-400334 19890207; ES 2057157 T3 EP 1989-400334 19890207;

CA 1336119 C CA 1989-590274 19890207; JP 2930965 B2 JP 1989-27744 19890208
FDT DE 68916820 E Based on EP 328446; ES 2057157 T3 Based on EP 328446; JP 2930965 B2 Previous Publ. JP 02152992
PRAI FR 1988-1439 19880208
AB EP 328446 A UPAB: 19930923
New conjugate (I) comprises a vinca (indoledihydroindole) deriv. having on C3 a 'detergent' chain of at least 7 aliphatic C bonded covalently to a natural polypeptide (II) as macromolecular carrier.

Pref. the chain has a terminal COOH for coupling, as peptide, to a free amino gp. in (II). Pref. (I) are of formula (7a) (R1,R2) = (Et,OH) or (H,Et) R4 = H, Me or CHO; R3 = OH or OCOMe; R = -A-R'-**CO**-; A = NH, NH-alk-COO, NH-alk-CONH-, or is the divalent residue of an amino acid present in proteins and endig in NH and COO or NH and CONH alk = opt. branched 1-7C aliphatic hydrocarbon chain; R' = gp. wlth at least 7 aliphatic C; R is substd. by **CO** (from terminal COOH) and is coupled to free amino in T via CONH; T = residue of (II); -RT can also be -A-R'-CONH-P, with NHP = T.

USE/ADVANTAGE - (I) are useful as anticancer agents having (compared with the free alkaloids) better selectivity and activity, and lower inherent toxicity. Component (II) provides targetted delivery to the cancer cells; e.g., where (II) is galactosylated human **albumin** (GHA) the conjugate is specific for hepatocytes and human hepatoma cells. 0/3

L27 ANSWER 12 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1988-279549 [40] WPIDS
DNN N1988-212193 DNC C1988-124441
TI Low mol. wt. mimic of superoxidedismutase - comprises water-soluble complex formed between chelating agent and **manganese**, used for treating inflammation, etc..
DC B05 C03 P34
IN DARR, D J; FRIDOVICH, I
PA (UYDU-N) UNIV DUKE
CYC 15
PI EP 284645 A 19881005 (198840)* EN 12p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
JP 63250392 A 19881018 (198847)
US 5223538 A 19930629 (199327) 6p
ADT EP 284645 A EP 1987-106684 19870508; JP 63250392 A JP 1987-120335 19870519; US 5223538 A US 1987-32475 19870331
PRAI US 1987-32475 19870331
AB EP 284645 A UPAB: 19930923
A low mol. wt. mimic of superoxide dismutase is claimed comprising a water-soluble complex formed between a chelating agent and **manganese**, the complex being capable of catalysing the dismutation of superoxide radicals and capable of retaining its activity in the presence of proteins.

Suitable chelating agents are siderophores, pref. of the hydroxamate type, esp. desferrioxamine or an analogue or deriv.

USE - The mimic catalyses the dismutation of 02(-) and retains its activity in the presence of serum **albumin** and cellular extracts contg. protein. It is useful for treating inflammation, extending the storage lifetime of organs and tissues intended for transplantation, decreasing damage to the heart suffered as a consequence of infarction, protecting against tissue death and necrosis following any situation entailing temporary cessation of circulation to a tissue or organ, as a radioprotectant and as an antioxidant applicable to any **free radical** chain oxidation in which 02(-) serves either as initiator or chain propagator. It may also be useful in inhibiting autoxidation reactions, thus providing increased shelf life for e.g. food prod.,

pharmaceuticals and stored blood. It may also be used for protecting plant cells from the toxicity of superoxide radicals.
0/2

L27 ANSWER 13 OF 13 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1986-126270 [20] WPIDS
CR 1984-213350 [34]; 1986-056863 [09]; 1986-056864 [09]; 1989-007515 [01]; 1991-021596 [03]; 1991-332540 [45]; 1996-208134 [20]
DNC C1986-053835
TI High purity immunoglobulin G prodn. from animal plasma - by filtration-adsorption and ion exchange chromatography esp. when transferrin and **albumin** are also isolated.
DC A96 B04
IN COGSWELL, G
PA (AMMA) AMF INC; (CUNO-N) CUNO INC; (HOUK-I) HOU K C; (HOUK-I) HOU K C
CYC 13
PI EP 180766 A 19860514 (198620)* EN 154p
R: AT BE CH DE FR GB IT LI LU NL SE
JP 61087631 A 19860506 (198624)
US 4639513 A 19870127 (198706)
ADT EP 180766 A EP 1985-112468 19851002; JP 61087631 A JP 1985-216307 19851001; US 4639513 A CIP of US 1983-466114 19830214, CIP of US 1984-576448 19840202, CIP of US 1984-643212 19840822, CIP of US 1984-643613 19840822, US 1984-656922 19841002
PRAI US 1984-656922 19841002; US 1983-466114 19830214; US 1984-576448 19840202; US 1984-643212 19840822; US 1984-643613 19840822
AB EP 180766 A UPAB: 19960604
(1)Prodn. of high purity immunoglobulin G(IgG) from animal plasma comprises (a) diluting the plasma; (b) sepng.sparingly soluble and insoluble plasma components by filtration/adsorption, so that the adsorbability of proteolytic enzymes is potentiated, to give extraneous protein-contg. IgG; and (c) sepng. the IgG from the protein-contg. IgG by ion-exchange chromatography, opt. followed by affinity chromatography.
(2)Continuous prodn. of IgG, transferrin (I) and **albumin** (II) from animal plasma comprises (a) diluting the plasma; (b) filtering/adsorbing the plasma to separate sparingly soluble and pptd. plasma components to give a first filtrate; (c) passing the filtrate through a first ion-exchange column to give an adsorbed fraction and an unadsorbed fraction. The adsorbed fraction contains (I) and (II) and some IgG, and the unadsorbed fraction contains most of the IgG; (d) eluting the (I) and part of the (II); (e) eluting the remaining (II); and (f) using a further series of adsorptions on ion-exchange resins and elutions to give the prods.

USE/ADVANTAGE - High purity IgG suitable for intravenous injection is obtd. in high yields. The prod. is remarkably free from aggregates, fragments,proteolytic enzymes, enzyme activators, coagulating factors etc., and it has much reduced anticomplementary activity. Highly pure (I) and (II) may also be obtd. The IgG is injected into humans to give high levels of antibodies, so that they can combine specifically with antigens such as viruses and bacteria.
0/0
Dwg.0/0